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(54) **Identification method and specific detection method of slow growing mycobacteria utilizing DNA gyrase gene**

(57) A method for identification and detection of slow growing mycobacteria, especially tubercle bacilli group bacteria, utilizing characteristic nucleotide sequences which are present in the *gyrB* gene. It renders possible accurate identification and detection of slow growing mycobacteria which are difficult by the conventional methods.

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Description

FIELD OF THE INVENTION

5 [0001] The present invention relates to a method for identification or detection of slow growing mycobacteria having a large number of clinical cases as causative microorganisms of tuberculosis and atypical mycobacterial disease (especially, tubercle bacilli group bacteria), which utilizing a nucleotide sequence of a DNA coding for DNA gyrase β subunit (to be referred to as "gyrB gene" or "gyrB" hereinafter). The identification and detection methods of the present invention are useful in various industrial fields, such as medical science, immunology and veterinary science.

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BACKGROUND ART

[0002] A plurality of species belonging to slow growing mycobacteria are known as acid-fast bacterial species which cause tuberculosis and diseases analogous to tuberculosis in human. Among all, *Mycobacterium tuberculosis* complex, *Mycobacterium avium* complex and *Mycobacterium kansasii* occupy the most part of clinical cases. Recently, these bacteria are causing a serious problem for the prognosis of patients of acquired immunodeficiency syndrome (AIDS), because they induce systemic disseminated infection in AIDS patients.

[0003] Conventionally, identification and detection of these bacterial species have been carried out by physiological and biochemical methods based on the culturing. For example, identification and detection have been carried out using 20 such differences in color development because (1) since there are three groups in the slow growing mycobacteria, namely a group which develops yellow color only when it is cultured in the dark after irradiation with light (photochromogen), (2) a group which develops color even when cultured without irradiation of light (scotochromogen) and (3) a group which does not develop color even when light is irradiated (achromogen). Known methods include identification and detection based on the ability of cultured bacteria to produce catalase or show urease activity, Tween hydrolyzing 25 activity or nitrate reducing activity.

[0004] Tuberculosis is a most important infectious disease, because ninety million people in the world newly contract the disease every year and thirty million people of them die every year, but its countermeasure is not sufficient. Tubercle bacilli as its causative agents are classified into four strains, namely a tubercle strain (*Mycobacterium tuberculosis*), a bovine type strain (*Mycobacterium bovis*) and an Africa strain (*Mycobacterium africanum*) which are 30 pathogenic for human and a rat type strain (*Mycobacterium microti*) which is not pathogenic for human. Conventionally, tests of acid-fast bacteria including these mycobacteria were mainly carried out by smear staining by the Ziehl-Neelsen method, isolation culturing method using Ogawa medium and a drug-sensitivity test. With the development of techniques thereafter, BACTEC 460 TB System, Septi-Check AFB, MGIT (*Mycobacteria Growth Indicator Tube*) and the like novel culture techniques have been developed.

35 [0005] However, these tests require pure culture. In addition, because phenotype to be compared is liable to change, the judgment often becomes subjective. As a result, not only a prolonged period of time is required but also accurate judgment of the species is extremely difficult. In order to solve such problems, certain identification and detection methods have recently been considered and put into use, e.g., a method for judging the presence of a specific nucleotide sequence of a gene utilizing the polymerase chain reaction (to be referred to as "PCR" hereinafter) or the 40 like, sub-classification of mycobacteria using an insertion sequence IS6110, and the like. The PCR method is suited for identifying and detecting slow growing mycobacteria from the viewpoint that quick and objective judgment is possible without requiring culturing.

[0006] In that case, the gene to be used is a rRNA gene in most cases. T. Rogall *et al.* (1990, *J. Gen. Microbiol.*, 136, 1915 - 1920) have proposed a method for the identification of mycobacteria species based on PCR using 16S 45 rRNA sequences. However, these primers could not distinguish between *Mycobacterium gastr* and *Mycobacterium kansasii*, which show different phenotype characteristics. On the other hand, B. Boddington *et al.* (1990, *J. Clin. Microbiol.*, 28: 1751 - 1759) have reported an oligonucleotide derived from 16S rRNA sequence, which is specific for human type mycobacterium group, avian type mycobacterium-paramycobacterium and *Mycobacterium intracellulare* group. Even the use of this oligonucleotide could not give necessary resolution for carrying out identification at species 50 level. An identification method using these rRNA gene sequences is now on the market and available from Nippon Roche as a gene diagnosis kit under a trade name of "Amplicore Mycobacterium". In addition to this, detection or identification methods using rRNA sequences have been disclosed by Toyobo (JP-A-10-323189; the term "JP-A" as used herein means an "unexamined published Japanese patent application") and Becton, Dickinson and CO. (JP-A-10-057098). In order to solve the aforementioned problem of not being able to distinguish two species, an identification or 55 detection method using the sequence of a region between 16S rRNA and 23S rRNA has been proposed by A. Roth *et al.* (1998, *J. Clin. Microbiol.*, 36: 139 - 147). However, since the region between 16S rRNA and 23S rRNA has only about 200 base pairs, it is difficult to carry out high accuracy molecular phylogenetic analysis by such a short sequence, and, when a new strain having an intermediate sequence which does not coincide with any one of the sequences of two

strains is generated, it is not able to judge its closeness to which of them.

[0007] On the other hand, it was shown that more minute and accurate classification and identification of many bacteria including those of the genus *Pseudomonas* and the genus *Acinetobacter* is possible by using a gene which encodes a protein having high evolution rate, particularly a 1,200 bp sequence of *gyrB* gene (Yamamoto, S. and S. Harayama, 1995, *Appl. Environ. Microbiol.*, 61: 1104 - 1109, Yamamoto, S. and S. Harayama, 1996, *Int. J. Syst. Bacteriol.*, 46: 508 - 511, Harayama, S. and S. Yamamoto, 1996, pp. 250 - 258 In *Molecular Biology of Pseudomonas*, T. Nakazawa, K. Fukuda, D. Haas, S. Silver (eds), ASM Press, Washington, D.C., S. Yamamoto and S. Harayama, *Kagaku-to-Seibutsu* (Chemistry and Biology, Japan), 1996, vol. 34, no. 3, pp. 149 - 151, S. Yamamoto and S. Harayama, *Nippon Nogei Kagaku Kaishi* (Journal of Agricultural Chemistry, Japan), 1997, vol. 71, no. 9, pp. 894 - 897).

[0008] Attempts have been made to carry out identification of slow growing mycobacteria using genes coding for proteins other than the *gyrB* gene. For example, C.T. Shivannvar *et al.* have discussed on the phylogenetic relationship among slow growing mycobacteria and their relationship to antigenicity using superoxide dismutase gene (1994, *J. Clin. Microbiol.*, 32: 2801 - 2812), and D.S. Swanson *et al.* have attempted to carry out minute classification of avian type mycobacterium-paramycobacterium and *Mycobacterium intracellulare* group using a 65 kD heat shock protein gene (1997, *Int. J. Syst. Bacteriol.*, 47: 414 - 419). In addition to the rRNA gene, Abbott Laboratories, USA, has disclosed a detection method which uses a gene coding for a protein antigen B of *Mycobacterium tuberculosis*, gene sequences of 65 kD heat shock protein, 10-kD heat shock proteins and the like of *Mycobacterium tuberculosis* and sequences related to insertion sequences IS987 and IS6110, in JP-W-10-500567 (the term "JP-W" as used herein means an "Japanese national publication of a PCT application") (International Publication No. WO 95/31571). In addition, Becton, Dickinson and Co. has disclosed in JP-A-06-319560 a detection or identification probe derived from a gene which encodes a 70 kD heat shock protein of *Mycobacterium paratuberculosis*. However, among these genes, only the *gyrB* gene shows no contradiction when molecular phylogenetic data are compared with the identification of species by the conventional taxonomic means (Yamamoto and Harayama, 1998, *Int. J. Syst. Bacteriol.*, 48: 813 - 819, Yamamoto *et al.*, 1999, *Int. J. Syst. Bacteriol.*, 49: 87 - 95, Suzuki *et al.*, *Int. J. Syst. Bacteriol.*, in press, Kasai *et al.*, *Int. J. Syst. Bacteriol.*, in press).

[0009] A patent application relating to a method for the identification or detection of bacteria using the *gyrB* gene has already been filed by the present applicant (JP-A-11-16917). However, this document does not disclose identification and detection of slow growing mycobacteria and also does not teach or suggest which region of the *gyrB* gene can be used in carrying out identification and detection of slow growing mycobacteria.

[0010] Because the slow growing mycobacteria include the bacteria that cause tuberculosis and the like serious diseases, great concern has been directed toward the development of a method for accurately identifying and detecting this bacterial group. On the other hand, because the growth rate of slow growing mycobacteria is lower than that of general bacteria, it is difficult to identify or detect them by physiological and biochemical methods which essentially require culturing of bacteria.

[0011] The present invention has been accomplished under such technical background to provide a method for the identification or detection of slow growing mycobacteria, especially tubercle bacilli group bacteria, utilizing the *gyrB* gene.

[0012] With the aim of solving the aforementioned problems, the present inventors have conducted extensive studies and, as a result, found that at least a part of the nucleotide sequence of *gyrB* DNA is different among the slow growing mycobacteria.

[0013] The present inventors further determined *gyrB* gene sequences of standard strains of the slow growing mycobacteria. Taxonomic positioning of strains isolated from clinical cases was carried out based on these sequences. Then, the resulting taxonomic positioning was checked by the DNA-DNA hybridization method, which is a standard method for identifying species of bacteria. As a result, it was unexpectedly found that the taxonomic positioning determined by using *gyrB* gene sequences shows good agreement with the result of the conventional classification method.

[0014] In addition, nucleotide sequences of *gyrB* fragments were determined by the PCR method by amplifying them from DNA samples of standard strains of atypical mycobacteria, *Mycobacterium gastri* and *Mycobacterium kansasii*, which cannot be distinguished by the nucleotide sequence of 16S rRNA gene which is the most generally used gene sequence-aided detection method of bacteria. When the resulting sequences were compared, it was found that the 16S rRNA gene sequence was identical in both strains, but 66 positions in the 1,257 base *gyrB* gene nucleotide sequence were different in both strains (Figs. 1-11). The present inventors further found that the taxonomically near bacteria belonging to the slow growing mycobacteria can be distinguished by designing primers based on such difference in their sequences, which renders possible the PCR amplification specific for each of these strains. Thus, the present inventors found that it can determine accurate molecular phylogenetic position of even a newly isolated strain and also can distinguish related species which cannot be distinguished by other genes, so that it is a method superior to methods by other genes.

[0015] The present invention has been accomplished based on the above knowledge.

SUMMARY OF THE INVENTION

[0016] Thus, the present invention relates to a method for identifying slow growing mycobacteria, especially tubercle bacilli group bacteria, which comprises carrying out identification of bacteria using *gyrB* DNA as a marker. Also, the present invention relates to a method for detecting slow growing mycobacteria, especially tubercle bacilli group bacteria, which comprises carrying out detection of bacteria using *gyrB* DNA as a marker.

[0017] The present invention further relates to a method for identifying slow growing mycobacteria, which comprises amplifying the regions corresponding to SEQUENCE NO. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39 in the *gyrB* of slow growing mycobacteria, comparing nucleotide sequences of the amplified fragments with the nucleotide sequences described in SEQUENCE NO. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39, thereby calculating genetic distance from each sequence, and carrying out identification of the aforementioned slow growing mycobacteria based on the genetic distance.

[0018] Also the present invention relates to a method for detecting a specific bacterium belonging to the slow growing mycobacteria using a specific sequence in the *gyrB*. In particular, the present invention relates to a method for detecting *Mycobacterium kansasii*, which comprises detecting *Mycobacterium kansasii* using, as a primer or probe, an oligonucleotide that contains a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 4, or its complementary sequence, and also substantially functions as a primer or probe, and to a *Mycobacterium kansasii* detection kit which comprises the just described oligonucleotide.

[0019] The present invention also relates to a method for detecting *Mycobacterium gastri*, which comprises detecting *Mycobacterium gastri* using, as a primer or probe, an oligonucleotide that contains a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 6, or its complementary sequence, and also substantially functions as a primer or probe, and to a *Mycobacterium gastri* detection kit which comprises the just described oligonucleotide.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020]

Figs. 1 through 11 show alignment of the nucleotide sequences of various slow growing mycobacteria. The symbols at the left side in the figure indicate the organisms shown below.

KPM1403	<i>Mycobacterium simiae</i>
KPM1201	<i>Mycobacterium marinum</i>
KPM2201	<i>Mycobacterium gordonae</i>
ATCC25274	<i>Mycobacterium asiaticum</i>
KPM2027	<i>Mycobacterium scrofulaceum</i>
KPM2403	<i>Mycobacterium szulgai</i>
KPM3012	<i>Mycobacterium avium</i>
Bovine10	<i>Mycobacterium paratuberculo</i>
KPM3101	<i>Mycobacterium intracellulare</i>
KPM3401	<i>Mycobacterium malmoeense</i>
ATCC51789	<i>Mycobacterium branderi</i>
T801	<i>Mycobacterium africanum</i>
T901	<i>Mycobacterium microti</i>
T704	<i>Mycobacterium bovis</i>
T021	<i>Mycobacterium tuberculosis</i>
KPM3504	<i>Mycobacterium gastri</i>
KPM1001	<i>Mycobacterium kansasii</i>

Fig. 12 shows a result of the identification using the primers based on SEQUENCE No. 1, SEQUENCE NO. 3, and SEQUENCE No. 5. Panel A shows amplified results using *Mycobacterium kansasii*-specific primers (SEQUENCE NO. 1 and SEQUENCE NO. 3), and panel B using *Mycobacterium gastri*-specific primers (SEQUENCE NO. 1 and SEQUENCE NO. 5). Lanes 1 and 12 are molecular weight markers. Lanes 2: strain KPM 1001T, 3: strain KPM 1004, 4: strain KPM 1007, 5: strain KPM KY256, 6: strain KPM KY761, 7: strain KPM KY798, 8: strain KPM 1998-1, 9: strain KPM 3504T, 10: strain KPM 3502 and 11: strain KPM 3503.

Fig. 13 shows a phylogenetic tree of slow growing mycobacteria prepared by the molecular phylogenetic analysis. This figure shows an example in which the presence of new species of slow growing mycobacteria was shown by *gyrB* sequence analysis. By carrying out molecular phylogenetic analysis and comparing the thus obtained *gyrB*

sequences with already known *gyrB* sequences, it was shown that a group of strains KPM 2212, 2014, 1988-5, 2209 and 2013 are new species.

Fig. 14 is an electrophoresis photograph of products amplified by PCR using primers specific for bacteria which constitute the tubercle bacilli.

5 Fig. 15 is an electrophoresis photograph of products amplified by PCR using primers specific for each bacterium which constitutes the tubercle bacilli.

Fig. 16 is an electrophoresis photograph of fragments prepared by digesting PCR products with restriction enzymes.

10 DETAILED DESCRIPTION OF THE INVENTION

[0021] The following describes the present invention in detail.

[0022] As the first step for the detection or identification of the slow growing mycobacteria (especially tubercle bacilli group bacteria), a sample for detection or identification is collected. Examples of the sample include a sample collected from organisms (human, animals, etc.) showing tuberculosis or tuberculosis-analogous symptoms as well as a strain isolated from the sample. Examples of tuberculosis or tuberculosis-analogous symptoms include pneumonia, empyema, cystitis, pyelonephritis, prostatitis, peritonitis, pericarditis, meningitis, encephalitis, etc. (Pocket guide to clinical microbiology 2nd edition, Oatrick R. Murray, ASM press). The collected sample may be cultured or the microorganism in the sample may be isolated and cultured for the use in the following steps. However, the present invention is advantageous in that the sample as it is can be used.

[0023] Then, a sample or isolated microorganism is usually subjected to a treatment to destroy the cell to extract DNA from the cell. The method for this treatment is not particularly limited and includes physically destroying method, chemically destroying method, etc.

[0024] The sequence of the DNA gyrase β subunit in the sample is determined by using the conventional way. Examples of the method for determining the DNA sequence include the dideoxy terminator method (Molecular Cloning: a laboratory manual 2nd edition, J. Sambrook, E. F. Fritsch, T. Maniatis, CSH press). The sequence determined is compared with the sequences of the DNA gyrase β subunit of the slow growing mycobacteria (Sequence No. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39) to determine whether the microorganism in the sample belongs to the one of these slow growing mycobacteria or is a new species. For the determination, 85% to 100% homology with respect to the 1200 bp sequence of the DNA gyrase β subunit means the same species, while the homology less than 85% means a new species. As a surprising matter, the identification of the slow growing mycobacteria based on the DNA gyrase β subunit well matches with the identification of the slow growing mycobacteria by the conventional method. Thus, the present invention makes it possible to identify the slow growing mycobacteria in an accurate way and also makes it possible to distinguish the related species, which are not possible by the conventional way.

[0025] Without determining the whole sequence of the DNA gyrase β subunit, identification and detection of the slow growing mycobacteria according to the present invention can be carried out by utilizing one or more unique partial sequence in the DNA gyrase β subunit which is characteristic to one or more of the microorganisms belonging to the slow growing mycobacteria or related species thereof. Example of the unique sequence is a sequence having 0 or more, preferably at least 1, more preferably at least 2, and most preferably at least 3 unique bases in the sequence having a length of 5-mer to 50-mer, preferably 10-mer to 40-mer, more preferably 15-mer to 30-mer. When the unique sequence does not have a unique base, at least one unique base should exist at the 3'-side or 5'-side nearest neighbor base to the unique sequence. The complementary sequence to the unique sequence can be also used.

[0026] The unique base means a base which can be found in only one or only several related species among the slow growing mycobacteria. The unique base may be located at arbitrary position in the unique sequence. When the unique sequence is utilized as a primer for the PCR, a unique base located near the 3'-end is preferable for the 5'-end primer and a unique base located near the 5'-end is preferable for the 3'-end primer. For the method utilizing the gel electrophoresis described below, the unique sequence may be designed so that the 3'-side or 5'-side nearest neighbor base to the unique sequence is the unique base (i.e., the unique base is not contained in the unique sequence). Even if a unique sequence which is unique to a certain one species among the slow growing mycobacteria is not found, identification or detection of the certain species is possible by using in combination two or more unique sequences which are respectively unique to several species among the slow growing mycobacteria. For example, four tubercle bacilli group bacteria can be identified or detected by using Sequence 41 shown in Fig. 1. By using Sequence 55 in combination of Sequence 41, it is possible to identify or detect *Mycobacterium microti*, *Mycobacterium kansasii* and *Mycobacterium gastri* can be identified or detected by using Sequence 1 shown in Fig. 1. By using Sequence 3 in combination of Sequence 1, it is possible to identify or detect *Mycobacterium kansasii*. According to the present invention, a sample obtained from human or animals showing tuberculosis or tuberculosis-analogous symptoms is used. Accordingly, it is possible to avoid pseudo positive reaction even if there are microorganisms other than slow growing mycobacteria that have the same unique sequence in the DNA gyrase β subunit.

[0027] Examples of the concrete methods for identifying or detecting the slow growing mycobacteria, which utilizes the unique sequence, a partial sequence in the unique sequence, or a sequence having a unique sequence, in the DNA gyrase β subunit include (1) DNA chip (DNA microarray) (Gingeras et al., 1998, Genome Res. 8: 435-448; Troesch et al. 1999 J. Clin. Microbiol. 37: 49-55), (2) PCR using the same as primers (Kasai, H., Ezaki, T., Harayama, S. 2000. J. Clin. Microbiol. 38: 301-308), (3) hybridization using the same as a probe (de los Reyes et al. 1997. Appl. Environ. Microbiol. 63: 11007-1117), (4) cleavage by the restriction enzyme that recognizes the unique sequence (Kasai H., Ezaki, T., Harayama, S. 2000. J. Clin. Microbiol. 38: 301-308), and the like. Examples of the method to confirm the result of these methods include a method to confirm the existence of the amplified or cleaved fragments by the gel electrophoresis, a method using DNA chip (DNA microarray), etc. The above-described methods can be carried out by the known way (cf. Molecular Cloning: a laboratory manual 2nd edition, J. Sambrook, E. F. Fritsch, T. Maniatis, CSH press; Current protocols of molecular biology edited by Ausubel et al. Wiley; PCR primer - A laboratory manual. edited by Diefenbach & Dveksler. SCH press, all herein incorporated by reference) The identification method and the detection method according to the present invention are further described below.

(1) Identification method

[0028] The method of the present invention for identifying slow growing mycobacteria is characterized in that the regions corresponding to SEQUENCE NOS. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39 in the *gyrB* of slow growing mycobacteria are amplified by PCR, nucleotide sequences of the amplified fragments are compared with the nucleotide sequences described in SEQUENCE NOS. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39, thereby calculating genetic distance from each sequence, and then identification of the aforementioned slow growing mycobacteria is carried out based on the genetic distance.

[0029] The term "identification" as used herein means that taxonomic positions of bacteria are determined by a molecular phylogenetic or the like means.

[0030] Though not particularly limited, the primers represented by SEQUENCE NO. 59 and SEQUENCE NO. 60 can be exemplified as the primers to be used in the amplification of the regions corresponding to SEQUENCE NOS. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39 in the *gyrB*.

[0031] Relationship between the nucleotide sequences of SEQUENCE NOS. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39 and their corresponding amino acid sequences and names of original microorganisms is shown in the following table.

TABLE 1

Nucleotide sequence	Amino acid sequence	Name of original microorganisms
SEQUENCE NO. 7	SEQUENCE NO. 8	<i>Mycobacterium simiae</i>
SEQUENCE NO. 9	SEQUENCE NO. 10	<i>Mycobacterium bovis</i>
SEQUENCE NO. 11	SEQUENCE NO. 12	<i>Mycobacterium szulgai</i>
SEQUENCE NO. 13	SEQUENCE NO. 14	<i>Mycobacterium malmoeense</i>
SEQUENCE NO. 15	SEQUENCE NO. 16	<i>Mycobacterium intracellulare</i>
SEQUENCE NO. 17	SEQUENCE NO. 18	<i>Mycobacterium avium</i>
SEQUENCE NO. 19	SEQUENCE NO. 20	<i>Mycobacterium gordonae</i>
SEQUENCE NO. 21	SEQUENCE NO. 22	<i>Mycobacterium africanum</i>
SEQUENCE NO. 23	SEQUENCE NO. 24	<i>Mycobacterium tuberculosis</i>
SEQUENCE NO. 25	SEQUENCE NO. 26	<i>Mycobacterium gastri</i>
SEQUENCE NO. 27	SEQUENCE NO. 28	<i>Mycobacterium marinum</i>
SEQUENCE NO. 29	SEQUENCE NO. 30	<i>Mycobacterium microti</i>
SEQUENCE NO. 31	SEQUENCE NO. 32	<i>Mycobacterium asiaticum</i>
SEQUENCE NO. 33	SEQUENCE NO. 34	<i>Mycobacterium scrofulaceum</i>
SEQUENCE NO. 35	SEQUENCE NO. 36	<i>Mycobacterium branderi</i>
SEQUENCE NO. 37	SEQUENCE NO. 38	<i>Mycobacterium paratuberculosis</i>

TABLE 1 (continued)

Nucleotide sequence	Amino acid sequence	Name of original microorganisms
SEQUENCE NO. 39	SEQUENCE NO. 40	<i>Mycobacterium kansasii</i>

[0032] The genetic distance can be calculated in accordance, for example, with the method described by Felsenstein in the Phylip program (Felsenstein, J., 1993 PHYLIP (Phylogeny Inference Package) version 3.5c. Distributed by the author, Department of Genetics, University of Washington, Seattle, U.S.A.).

(2) Specific detection

[0033] The method of the present invention for detecting *Mycobacterium kansasii* is characterized by the use, as a primer or probe, of an oligonucleotide which contains a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 4, or its complementary sequence, and functions substantially as a primer or probe. Also, the *Mycobacterium kansasii* detection kit of the present invention is characterized in that it contains the just described oligonucleotide.

[0034] The method of the present invention for detecting *Mycobacterium gastr* is characterized by the use, as a primer or probe, of an oligonucleotide which contains a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 6, or its complementary sequence, and also functions substantially as a primer or probe. Also, the *Mycobacterium gastr* detection kit of the present invention is characterized in that it contains the just described oligonucleotide.

[0035] In this connection, the term "substantially functions as a primer or probe" means that the oligonucleotide has such a length that a specific annealing or hybridization can be effected, and its gist is to exclude the oligonucleotide which has a sequence that can anneal to or hybridize with the DNA to be detected but cannot be used in specific detection, because it frequently causes nonspecific annealing or hybridization due to its short length. In order to confirm that a certain oligonucleotide can substantially functions as a primer for PCR, the PCR is carried out at a 3°C higher annealing temperature and a 3°C lower annealing temperature than the usually employed temperature for the PCR. If the PCR product is observed only at 3°C lower annealing temperature, there is a possibility of false-positive. In such a case, the nucleotide sequence of the amplified fragment is determined by the conventional way and compared with the known sequence to confirm whether the oligonucleotide used can substantially work as a primer. In order to confirm that a certain oligonucleotide can substantially function as a primer for PCR, it is preferable to perform PCR by using DNA of already known strain (for example, type strain) as a template for positive and negative controls.

[0036] Though not particularly limited, the oligonucleotide represented by SEQUENCE NO. 3 can be exemplified as an oligonucleotide which can be used in the detection of *Mycobacterium kansasii*, and the oligonucleotide represented by SEQUENCE NO. 5 can be exemplified as an oligonucleotide which can be used in the detection of *Mycobacterium gastr*.

[0037] Preparation of DNA to be tested, preparation of primers and PCR using the same, and preparation of probes and hybridization using the same can be carried out in the usual way without requiring special techniques.

[0038] Regarding the primers to be used in PCR, it is not always necessary that both of them can perform specific annealing, and one of them may perform nonspecific annealing. The primer represented by SEQUENCE NO. 1 can be cited as an example of such a primer which performs nonspecific annealing.

[0039] The methods of the present invention for identifying and detecting the slow growing mycobacteria (especially, tubercle bacilli group bacteria) are characterized in that *gyrB* DNA is used as a marker. Examples of the slow growing mycobacteria include those shown in Table 1. Examples of the tubercle bacilli group bacteria include *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum* and *Mycobacterium microti*.

[0040] The following four methods can be exemplified as the identification and detection methods which use *gyrB* DNA as a marker.

A) A method which employs PCR

[0041] This method is carried out as follows.

(1) An oligonucleotide which contains a region of *gyrB* DNA, a region that has different nucleotide sequence among tubercle bacilli group bacteria, is synthesized. Since the nucleotide sequence of *gyrB* DNA corresponding to each bacterium is already determined as shown in Figs. 1-11, the just described oligonucleotide can be synthesized based on these drawings. As the oligonucleotide, an oligonucleotide which encodes the amino acid sequence described in SEQUENCE NO. 46, SEQUENCE NO. 48, SEQUENCE NO. 50, SEQUENCE NO. 52, SEQUENCE NO. 54, SEQUENCE NO. 56 or SEQUENCE NO. 58 can be exemplified as a preferable oligonucleotide, and an oli-

gonucleotide represented by SEQUENCE NO. 45, SEQUENCE NO. 47, SEQUENCE NO. 49, SEQUENCE NO. 51, SEQUENCE NO. 53, SEQUENCE NO. 55 or SEQUENCE NO. 57 can be exemplified as a particularly preferable oligonucleotide.

(2) A solution which contains the oligonucleotide synthesized in the above step, dNTP, DNA polymerase and a bacterial DNA to be used as a sample is prepared. Concentration of each component contained in the solution may be the same as that in the reaction solution used in general PCR. It is not necessary to purify the bacterial DNA to be used as a sample, and disrupted cells may be used as such for example.

(3) The solution prepared in the above step is repeatedly heated under such conditions that PCR can be generated. The heating temperature, cycle and the like conditions are not particularly limited, with the proviso that they are within such ranges that PCR can be effected, but, since the homology of *gyrB* DNA among tubercle bacilli group bacteria is high as shown in Figs. 1-11, it is desirable to set the temperature at the time of annealing to a fairly high level. Illustratively, it is desirable to set at 68°C or more. When the synthesized oligonucleotide can be hybridized with the added bacterial DNA, PCR occurs by the repetition of heating and amplified product is formed thereby. On the other hand, when the synthesized oligonucleotide cannot be hybridized with the added bacterial DNA, PCR does not occur and amplified product is not formed.

(4) Electrophoresis of the solution after the above treatment is carried out. When the amplified product is contained in the solution, its corresponding band is formed on the electrophoresis gel. In consequence, identification and detection of the bacterium of interest can be made based on the electrophoresis pattern.

B) A method which uses restriction enzyme digestion fragments

[0042] This method is carried out as follows.

(1) An oligonucleotide which is identical to a part of *gyrB* DNA of tubercle bacilli group bacteria and a complementary oligonucleotide of the aforementioned part of DNA are synthesized. Since the nucleotide sequence of *gyrB* DNA corresponding to each bacterium is already determined as shown in Figs. 1-11, the best described oligonucleotides can be synthesized based on these drawings. As preferred oligonucleotides, an oligonucleotide which encodes the amino acid sequence described in SEQUENCE NO. 42 and an oligonucleotide which encodes the amino acid sequence described in SEQUENCE NO. 44 can be exemplified, and the oligonucleotide represented by SEQUENCE NO. 41 and the oligonucleotide represented by SEQUENCE NO. 43 can be exemplified as particularly preferred oligonucleotide.

(2) PCR is carried out using the two oligonucleotides synthesized in the above step as primers, and a bacterial DNA sample as a template. It is not necessary to purify the bacterial DNA to be used as a sample, and disrupted cells may be used as such for example. PCR can be carried out in the usual way.

(3) The DNA fragment amplified in the above step is digested with restriction enzymes. The restriction enzymes to be used are not particularly limited, with the proviso that they can generate different fragments among corresponding bacteria which constitute tubercle bacilli. For example, *Rsa* I and *Taq* I can be exemplified as such restriction enzymes.

(4) Electrophoresis of the fragments digested in the above step is carried out. The digested DNA fragments appear at positions corresponding to their length. In consequence, identification and detection of the bacterium of interest can be made based on the electrophoresis pattern.

[0043] The aforementioned two methods can be cited as typical examples of the identification or detection method of the present invention, but other methods are also included in the identification or detection method of the present invention, with the proviso that they use *gyrB* DNA as a marker. Examples of these other identification or detection methods include a method in which *gyrB* DNA is amplified by PCR, and identification or detection of the bacterium of interest is carried out by determining nucleotide sequence of the amplified fragment and a method in which an oligonucleotide which contains a region of *gyrB* DNA, a region that has different nucleotide sequence among tubercle bacilli group bacteria, is synthesized, and the bacterium of interest is identified or detected by carrying out Southern blotting using the oligonucleotide as a probe.

C) Method which employs the gel electrophoresis

[0044] According to this method, easy and qualitative analysis as well as a certain degree of quantitative analysis are possible for *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. microti*, *M. kansasii*, *M. avium*, *M. intracellulare* and for the multiple infection found in the patient having lowered immunological competence.

[0045] Dideoxy nucleotides and primers that are unique to one or more of these species are used for this method. The oligonucleotide used as a primer is designed so that the 3'-side nearest neighbor base in DNA gyrase β subunit

sequence to the primer is the unique base. The sequence of the primer itself may be common in all of the slow growing mycobacteria or may be common in one or more slow growing mycobacteria. In the latter case, an oligonucleotide mixture is preferably used in order to assure the reaction.

[0046] All of the 4 types of dideoxy nucleotides is labeled with a fluorescent substance or radioactive substance. By labeling each of the 4 dideoxy nucleotides with different types of substances, it is possible to obtain the necessary information from only one lane of the sequence gel. Labeling the 4 dideoxy nucleotides with the same fluorescent substance or radioactive substance requires to carry out electrophoresis using 4 different lanes.

[0047] The reaction mixture used for this method is the same with the reaction mixture for the usual sequence reaction except that dATP, dTTP, dGTP, and dCTP are not contained. In other words, the reaction mixture contains, as essential components, an appropriate buffer, a DNA polymerase, a labeled ddNTP, and the primer. A sample collected from the patient is mixed with this reaction mixture and then subjected to the reaction at an appropriate temperature at which the reaction can occur (for example, at 95°C for 10 seconds, 50°C for 5 seconds, and 60°C for 4 minutes; 25 cycles). Then, existence of the labeled primer is checked, for example, by subjecting the reaction product to the gel electrophoresis by the conventional way, or the like. The pattern which appears on the gel differs depending on the length of the primer used and the type of the 3'-side nearest neighbor based to the primer. The location of the primer sequence is not particularly limited as long as the length of the primer sequence is the same. However, for the quantitative analysis, primers having a quite high ΔT_m (about 5°C or more) is not preferable. Examples of the primers include the nucleotides represented by Sequence 61 (5'-gagcgctaygcgatatc-3') based on the *M. tuberculosis* complex and *M. kansasii* and Sequence 62 (5'-agcggytacaacgctag) based on *M. avium* and *M. intracellulare* in Fig. 1. At the position corresponding to the 18-base length, a signal of "T" is found in the case of *M. tuberculosis* complex, "G" for *M. kansasii*, and "C" for *M. intracellulare*. Detection of a plural number of signals at the position corresponding to the 18-base length means the multiple infection. Moreover, approximate amount of existence of each species can be estimated from the signal intensity detected. The sequence that is unique to 4 species of the tubercle bacilli group bacteria and the sequence which can distinguish *M. gastri* (a species which is near to *M. kansasii* but has only a few number of clinical cases of human infection) have been explained in the above-described methods. By combining this method which uses gel electrophoresis with the above-described methods, further detailed identification or detection is possible.

D) Method which employs the DNA chip

[0048] The detection or identification of the slow growing mycobacteria is also possible by utilizing the DNA chip. Examples of the method which employs the DNA chip is described below. First, the region in the DNA gyrase β subunit in one or more standard strains of the slow growing mycobacteria is amplified, for example, by the PCR. Then, the amplified product is labeled by Cy5 or the like, and the synthesized DNA oligo probe is fixed on a plate such as slide glass. A DNA in a sample is obtained and subjected to a hybridization reaction on the plate having a solid phrased probe, which is then subjected to washing and detection in the conventional way. The size of the region in the DNA gyrase β subunit is preferably 250 bp or less, more preferably 180 bp or less, and still more preferably 125 bp or less. The oligo probe size is preferably from 14 to 17 mer.

[0049] Known protocols for the method which employs the DNA chip can be employed for the above-described method (cf. Lemieux, B., Aharoni, A., and M. Schena (1998), Overview of DNA Chip Technology, Molecular Breeding, 4, 277-289; Schena, M., Heller, R.A., Theriault, T.P., Konrad, K., Lachenmeyer, E., and R.W. Davis (1998), Microarrays: biotechnology's discovery platform and functional genomics, Trends in Biotechnology, 18, 301-306; and Heller, R.A., Schena, M., Chai, A., Shalom, D., Bedilion, T., Gilmore, J., Woolley, D.E., and Davis, R.W. (1997), Discovery and analysis of inflammatory disease-related genes using cDNA microarrays, Proceedings of the National Academy of Sciences USA, 94, 2150-2155), all herein incorporated by reference).

[0050] Illustrative but non-limiting example of the protocol for the DNA chip method is described below.

(1) Labeling

[0051] PCR amplification product (125 bp) is obtained by 40-cycles treatment (each cycle: at 96°C for 1 minute, 55°C for 30 seconds, and 72°C, 2 minutes). The product is then subjected to the ethanol precipitation. Then, 10 μ M Cy5-dCTP/100 μ l is added instead of dCTP/100 μ l and the 40-cycles treatment was carried out again (each cycle: at 96°C for 1 minute, 55°C for 30 seconds, and 72°C, 2 minutes). Then, the product is subjected to the ethanol precipitation.

(2) Spotting

[0052] Spotting is carried out under the following conditions.

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Slide: Silylated Slides

Spotting: Spotting by SPBIO (manufactured by HITACHI) using a 4 Pin head with a pitch of 1.0 mm. A 20 µl sample (10 µl of 200 µM probe + 10 µl of x2 Spotting Solution (ArrayIt™)) is used for each well of the plate (about 4 to 5 nl per 1 spot).

5 Time: about 10 minutes/slide (96 spots)

Oligo probe size: conc. probe 14 - 17 mer, final conc. 100 µM

(3) Hybridization

10 [0053] Hybridization is carried out using UniHyb™ (ArrayIt™). The labeled product is dissolved in 4 µl of sterilized water and 16 µl of x1.25 UniHyb™ was added.

[0054] Then, 9.6 µl of the resulting mixture was dropped onto a cover slip (24 x 32 mm; 1.25 µl/cm²) and the cover slip was placed onto the microarray such that bubbles are not included between the cover slip and the microarray. Then, the microarray is incubated at 46°C for 4 hours.

15

(4) Washing

[0055] Washing is carried out with 2 x SSC (+ 0.2% SDS) for 5 minutes at room temperature, with 0.1 x SSC (+ 0.2% SDS) for 5 minutes at room temperature, and then with 0.1 x SSC (+ 0.2% SDS) for 5 minutes at room temperature. The microarray is centrifuged and dried. At least 1 week storage at 4°C is possible.

20

(5) Scanning

[0056] Scanning is carried out by using ScanArray 1000 (ScanArray Lite) manufactured by GSI LUMONICS.

25

Scanning software: ScanArray

Analyzing software: QuantArray

EXAMPLE 1

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[0057] Using the oligonucleotides represented by the nucleotide sequences described in SEQUENCE NO. 39 and SEQUENCE NO. 40, *gyrB* gene sequences of 8 acid-fast bacterial strains (KPM 2201T, KPM 2202, KPM 2203, KPM 2013, KPM 2014, KPM 1988-5, KPM 2209 and KPM 2212) isolated from clinical cases were determined. Using the thus obtained *gyrB* sequences and a *gyrB* sequence set (SEQUENCE NO. 7 to SEQUENCE NO. 40) for slow growing mycobacteria identification use, their phylogenetic relationship was estimated by a molecular phylogenetic analysis. The molecular phylogenetic analysis was carried out in the following manner using general-purpose molecular phylogenetic analysis programs Clustal W (Thompson, J.D., D.G. Higgins and T.J. Gibson, 1994, Clustal W: Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, positions-specific gap penalties and weight matrix choice., *Nucleic Acids Res.*, 22: 4673 - 4680) or Phylip (Felsenstein, J., 1993 PHYLIP (Phylogeny Inference Package) version 3.5c. Distributed by the author, Department of Genetics, University of Washington, Seattle, U.S.A.), in accordance with the instructions for use of both programs. A multiple alignment file is prepared by the Clustal W program from the *gyrB* gene sequences obtained using the oligonucleotides represented by the nucleotide sequences described in SEQUENCE NO. 59 and SEQUENCE NO. 60 and the slow growing mycobacteria identification *gyrB* sequence set of SEQUENCE NO. 7 to SEQUENCE NO. 40. An example of the parameters to be used in making the multiple alignment is "Gap Open Penalty: 15.00; Gap Extension Penalty: 6.66; DNA weight matrix: IUB; DNA transition weight: 0.5". The thus obtained multiple alignment is compared with a multiple alignment file obtained from amino acid sequences, and questionable points are corrected. Next, the genetic distance between respective sequences is calculated based on the multiple alignment file. The dnadist program of Phylip is used for the calculation. The calculation is carried out in accordance with the Kimura 2-parameter model. A phylogenetic tree is prepared from the thus obtained genetic distances by a neighboring sequences binding method. Correctness of the phylogenetic tree is checked by calculating the bootstrap probability.

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[0058] On the other hand, the aforementioned 8 strains were also identified by a 16S rRNA gene-aided method and a biochemical method. The above results are shown in Table 2.

55

TABLE 2

Strain name	Biological test	16S rRNA gene	DNA homology test
KPM 2201T	<i>M. gordonae</i>	<i>M. gordonae</i>	<i>M. gordonae</i>
KPM 2202	<i>M. gastri</i>	<i>M. gordonae</i>	<i>M. gordonae</i>
KPM 2203	<i>M. gastri</i>	<i>M. gordonae</i>	<i>M. gordonae</i>
KPM 2013	<i>M. scrofulaceum</i>	<i>M. gordonae</i>	new species
KPM 2014	<i>M. scrofulaceum</i>	<i>M. gordonae</i>	new species
KPM 1988-5	<i>M. scrofulaceum</i>	<i>M. gordonae</i>	new species
KPM 2209	<i>M. scrofulaceum</i>	<i>M. gordonae</i>	new species
KPM 2212	no data	<i>M. gordonae</i>	new species

[0059] As shown in the table, 3 of the above 8 strains, namely KPM 2201T, KPM 2202 and KPM 2203, were identified as strains belonging to *Mycobacterium gordonae*, but the other 5 strains, KPM 2013, KPM 2014, KPM 1988-5, KPM 2209 and KPM 2212, were suggested to be sibling species of *Mycobacterium gordonae* but different species (new species) (Fig. 13). When a DNA-DNA hybridization test (Ezaki, T., Hashimoto, Y., Takeuchi, T., Yamamoto, H., Shu-Lin Liu, Matsui, K. & Yabuuchi, E (1988), *J. Clin. Microbiol.*, 26, 1708 - 1713; Ezaki, T., Hashimoto, Y., Takeuchi & Yabuuchi, E (1989), *Int. J. Syst. Bacteriol.*, 39, 224 - 229) was carried out in order to inspect this result, it was supported that they are new species. This result suggests that the *gyrB* sequence set for slow growing mycobacteria identification use gives highly reliable results for not only known strains but also strains of new species.

EXAMPLE 2

[0060] Nucleotide sequences of the *gyrB* gene of *Mycobacterium kansasii* and *Mycobacterium gastri* (Figs. 1-11) were compared to prepare a primer which specifically anneals to the *gyrB* gene of *Mycobacterium kansasii* (SEQUENCE NO. 3) and a primer which specifically anneals to that of *Mycobacterium gastri* (SEQUENCE NO. 5). A primer which anneals to the *gyrB* gene of both strains (SEQUENCE NO. 1) was also prepared.

[0061] Using these primers, PCR was carried out on disrupted cell suspensions of strains KPM 1004, KPM 1007, KPM KY256, KPM KY761, KPM KY768, KPM 1998-1, KPM 3502 and KPM 3503 isolated from clinical cases.

[0062] The PCR amplification conditions are as follows.

At 95°C for 10 minutes; 1 cycle

At 95°C for 1 minute and 68°C for 1 minute and 30 seconds; 30 cycles

At 72°C for 10 minutes; 1 cycle

Primer concentration; 1 µM for each

dNTP: 100 µM for each

Ampli Taq GOLD™ and PCR buffer I attached thereto (Perkin Elmer, USA) were used.

[0063] When the thus amplified DNA fragments were analyzed by an electrophoresis, amplified fragments were observed only by the combination of SEQUENCE NO. 1 and SEQUENCE NO. 3 in the case of KPM 1004, KPM 1007, KPM KY256, KPM KY761, KPM KY768 and KPM 1998-1 (Table 3), so that these strains were identified as *Mycobacterium kansasii*. In the case of KPM 3502 and KPM 3503, amplified fragments were observed only by the combination of SEQUENCE NO. 1 and SEQUENCE NO. 5 (Table 3), so that these strains were identified as *Mycobacterium gastri*. The electrophoresis patterns used in the judgment are as shown in Fig. 12. These identification results coincided with the identification results of the DNA-DNA hybridization method.

TABLE 3

	<i>M. kansasii</i>	<i>M. gastri</i>
SEQUENCE NO. 1	amplification was possible	No amplification
SEQUENCE NO. 3		

TABLE 3 (continued)

	<i>M. kansasii</i>	<i>M. gastr</i>
SEQUENCE NO. 1	No amplification	amplification was possible
SEQUENCE NO. 5		

EXAMPLE 3

10 [0064] A 10 ng portion of purified DNA was prepared from each of 9 bacterial species including 4 tubercle bacilli group bacterial species and 5 other bacterial species belonging the genus *Mycobacterium*. PCR was carried out using these DNA samples as templates, and the oligonucleotides described in SEQUENCE NO. 41 and SEQUENCE NO. 43 as primers. The PCR amplification conditions are as follows.

15 At 95°C for 10 minutes; 1 cycle
 At 95°C for 1 minute, 68°C for 1 minute and 72°C for 1 minute; 30 cycles
 At 72°C for 10 minutes; 1 cycle
 Primer concentration; 1 µM for each
 dNTP: 100 µM for each
 20 Ampli Taq GOLD™ and PCR buffer 1 attached thereto (Perkin Elmer, USA) were used.

[0065] The products amplified by PCR were analyzed by an agarose gel electrophoresis. The results are shown in Fig. 14. In this connection, the relationship between lanes and bacterial species is as follows.

25 Lane 1: *Mycobacterium tuberculosis*
 Lane 2: *Mycobacterium bovis*
 Lane 3: *Mycobacterium africanum*
 Lane 4: *Mycobacterium microti*
 Lane 5: *Mycobacterium kansasii*
 30 Lane 6: *Mycobacterium gastr*
 Lane 7: *Mycobacterium abscessus*
 Lane 8: *Mycobacterium chelonae*
 Lane 9: *Mycobacterium triviale*

EXAMPLE 4

[0066] A 10 ng portion of purified DNA was prepared from each of 4 tubercle bacilli group bacterial species. PCR was carried out using these DNA samples as templates, and the oligonucleotides represented by SEQUENCE NO. 45, SEQUENCE NO. 47, SEQUENCE NO. 49, SEQUENCE NO. 51, SEQUENCE NO. 53, SEQUENCE NO. 55 and SEQUENCE NO. 57 as primers. The PCR amplification conditions are as described in Example 3. The products amplified by PCR were analyzed by an agarose gel electrophoresis. The results are shown in Fig. 15. In this case, the relationship between lanes and bacterial species is as follows.

45 Lane 1: *Mycobacterium tuberculosis*
 Lane 2: *Mycobacterium bovis*
 Lane 3: *Mycobacterium africanum*
 Lane 4: *Mycobacterium microti*

[0067] As shown in Fig. 15, the amplified product was observed only by *Mycobacterium tuberculosis* when the oligonucleotides represented by SEQUENCE NO. 45 and SEQUENCE NO. 47 were used as primers, the amplified product was observed only by *Mycobacterium bovis* when the oligonucleotides represented by SEQUENCE NO. 49 and SEQUENCE NO. 51 were used as primers, the amplified product was observed by *Mycobacterium africanum* and *Mycobacterium microti* when the oligonucleotides represented by SEQUENCE NO. 45 and SEQUENCE NO. 53 were used as primers and the amplified product was observed by only *Mycobacterium microti* when the oligonucleotides represented by SEQUENCE NO. 55 and SEQUENCE NO. 57 were used as primers. Based on the above results, relationship between primers and bacterial species can be summarized as follows.

TABLE 4

SEQUENCE No.	<i>Mycobacterium tuberculosis</i>	<i>Mycobacterium bovis</i>	<i>Mycobacterium africanum</i>	<i>Mycobacterium microti</i>
SEQ. NO. 41	Amplification possible	Amplification possible	Amplification possible	Amplification possible
SEQ. NO. 43				
SEQ. NO. 45	Amplification possible	No amplification	No amplification	No amplification
SEQ. NO. 47				
SEQ. NO. 49	No amplification	Amplification possible	No amplification	No amplification
SEQ. NO. 51				
SEQ. NO. 45	No amplification	No amplification	Amplification possible	Amplification possible
SEQ. NO. 53				
SEQ. NO. 55	No amplification	no amplification	no amplification	Amplification possible
SEQ. NO. 57				

EXAMPLE 5

[0068] A 10 ng portion of purified DNA was prepared from each of 4 tubercle bacilli group bacterial species. PCR was carried out using these DNA samples as templates, and the oligonucleotides represented by SEQUENCE NO. 41 and SEQUENCE NO. 43 as primers. The PCR amplification conditions are as described in Example 3. The products amplified by PCR were digested with restriction enzymes *Rsa* I and *Taq* I, and the thus formed DNA fragments were analyzed by an agarose gel electrophoresis. The results are shown in Fig. 16. In this connection, the relationship between lanes and bacterial species is as follows.

Lane 1: *Mycobacterium tuberculosis*
 Lane 2: *Mycobacterium bovis*
 Lane 3: *Mycobacterium africanum*
 Lane 4: *Mycobacterium microti*

EXAMPLE 6

[0069] Using the oligonucleotides represented by SEQUENCE NO. 1, SEQUENCE NO. 43, SEQUENCE NO. 45, SEQUENCE NO. 47, SEQUENCE NO. 49, SEQUENCE NO. 51, SEQUENCE NO. 53, SEQUENCE NO. 55 and SEQUENCE NO. 57 as primers, PCR was carried out on a solution of disrupted cells of a strain KPM KY631 isolated from a clinical patient of tuberculosis. When the product amplified by PCR was analyzed by an agarose gel electrophoresis, the amplified product was observed only by the combination of SEQUENCE NO. 1 and SEQUENCE NO. 43 and of SEQUENCE NO. 45 and SEQUENCE NO. 47, so that the strain KPM KY631 was identified as the tubercle *Mycobacterium tuberculosis* (Table 4 and Fig. 15).

EXAMPLE 7

[0070] Using the oligonucleotides represented by SEQUENCE NO. 41 and SEQUENCE NO. 43 as primers, PCR was carried out on a solution of disrupted cells of a strain KPM KY590 isolated from a clinical patient of tuberculosis. When nucleotide sequence of the thus amplified DNA fragment was determined, the thus obtained nucleotide sequence coincided with the nucleotide sequence of the tubercle *Mycobacterium tuberculosis*, so that the strain KPM KY590 was identified as the tubercle *Mycobacterium tuberculosis* (Figs. 1-11).

EXAMPLE 8

[0071] Using the oligonucleotides represented by SEQUENCE NO. 41 and SEQUENCE NO. 43 as primers, PCR was carried out on a solution of disrupted cells of a strain isolated from a bovine patient of tuberculosis. When the product amplified by PCR was digested with restriction enzymes *Rsa* I and *Taq* I and the thus formed DNA fragments were

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analyzed by an agarose gel electrophoresis, the result coincided with the pattern obtained from *Mycobacterium bovis*, so that this strain was identified as *Mycobacterium bovis* (Fig. 16).

5 [0072] The present invention realizes accurate classification and identification of slow growing mycobacteria which are difficult to identify by conventional methods. It also renders possible quick identification of certain species of atypical mycobacteria, such as *Mycobacterium kansasii* and *Mycobacterium gastri*, which are difficult to distinguish by the identification method based on 16S rRNA gene sequence. The present invention is useful in the fields of medical science, immunology, veterinary science, etc.

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SEQUENCE LISTING

5 <110> MARINE BIOTECHNOLOGY INSTITUTE CO., LTD.

<120> IDENTIFICATION METHOD AND SPECIFIC DETECTION METHOD OF
SLOW GROWING MYCOBACTERIA UTILIZING DNA GYRASE GENE

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Gly	Glu	Asn	Ser	Gly	Tyr	Thr	Val	Ser	Gly	Gly	Leu	His	Gly	Val	Gly	
1				5					10					15		

gtg	tcg	gtg	gtc	aac	gcc	ctg	tcc	acc	cgc	ctg	gaa	gtc	aac	gtc	aag	96
Val	Ser	Val	Val	Asn	Ala	Leu	Ser	Thr	Arg	Leu	Glu	Val	Asn	Val	Lys	
			20					25					30			

cgt	gac	ggc	tat	gag	tgg	ttc	cag	tac	tac	gac	cgg	gcg	gtg	ccc	ggc	144
Arg	Asp	Gly	Tyr	Glu	Trp	Phe	Gln	Tyr	Tyr	Asp	Arg	Ala	Val	Pro	Gly	
		35					40					45				

acc	ctc	aag	caa	ggc	gag	gcg	acc	aag	aag	acc	ggc	acc	acg	atc	cgg	192
Thr	Leu	Lys	Gln	Gly	Glu	Ala	Thr	Lys	Lys	Thr	Gly	Thr	Thr	Ile	Arg	

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5	ttc tgg gcc gat cct gag atc ttc gaa acc acc cag tac gac ttc gag Phe Trp Ala Asp Pro Glu Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu 65 70 75 80	240		
10	acg gtg gcg cgc cgg ttg cag gaa atg gcg ttc ctc aac aag ggc ctg Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu 85 90 95	288		
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	275	280	285	
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15	cgt aag agt gct acg gat ttg ggt ggg ttg ccg ggc aag ttg gct gat Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp 325 330 335			1008
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30	gcg atc ttg ccg ctg cgc ggc aag atc atc aac gtc gaa aag gcc cgc Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg 370 375 380			1152
35	atc gat cgg gtg ctg aaa aac acc gaa gtc cag gcc atc atc acc gcg Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala 385 390 395 400			1200
40	ctg ggc acc ggc atc cac gac gaa ttc gac atc acc aaa ctg cgt tac Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr 405 410 415			1248
45	cac aag atc gtg ttg His Lys Ile Val Leu 420			1263
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Phe Trp Ala Asp Pro Glu Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu
 65 70 75 80
 5 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 Thr Ile Asn Leu Thr Asp Glu Arg Val Glu Gln Asp Glu Val Val Asp
 100 105 110
 10 Glu Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Glu Glu Gln
 115 120 125
 Ala Ala Glu Ser Ala Lys Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140
 15 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160
 Asn Pro Ile Gln Gln Ser Val Ile Asp Phe Asp Gly Lys Gly Thr Gly
 165 170 175
 20 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
 180 185 190
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
 195 200 205
 25 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
 210 215 220
 Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240
 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu
 245 250 255
 35 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270
 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
 275 280 285
 40 Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser
 290 295 300
 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320
 45 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
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	370	375	380	
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35	ggg tac gag tgg tct cag gtt tat gag aag tcg gaa ccc ctg ggc ctc 144 Gly Tyr Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Leu Gly Leu 35 40 45			
40	aag caa ggg gcg ccg acc aag aag acg ggg tca acg gta cgg ttc tgg 192 Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp 50 55 60			
45	gcc gac ccc gct gtt ttc gaa acc acg gaa tac gac ttc gaa acc gtc 240 Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val 65 70 75 80			
50	gcc cgc cgg ctg caa gag atg gcg ttc ctc aac aag ggg ctg acc atc 288 Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile 85 90 95			
55	aac ctg acc gac gag agg gtg acc caa gac gag gtc gtc gac gaa gtg 336 Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val 100 105 110			
60	gtc agc gac gtc gcc gag gcg ccg aag tcg gca agt gaa cgc gca gcc 384 Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala 115 120 125			

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	gaa tcc act gca ccg cac aaa gtt aag agc cgc acc ttt cac tat ccg	432
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	Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala	
	145 150 155 160	
10	att cat agc agc atc gtg gac ttt tcc ggc aag ggc acc ggg cac gag	528
	Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu	
	165 170 175	
15	gtg gag atc gcg atg caa tgg aac gcc ggg tat tgc gag tgc gtg cac	576
	Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His	
	180 185 190	
20	acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac gaa gag	624
	Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu	
	195 200 205	
25	ggc ttc cgc agc gcg ctg acg tgc gtg gtg aac aag tac gcc aag gac	672
	Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp	
	210 215 220	
30	cgc aag cta ctg aag gac aag gac ccc aac ctc acc ggt gac gat atc	720
	Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile	
	225 230 235 240	
35	cgg gaa ggc ctg gcc gct gtg atc tgc gtg aag gtc agc gaa ccg cag	768
	Arg Glu Gly Leu Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln	
	245 250 255	
40	ttc gag ggc cag acc aag acc aag ttg ggc aac acc gag gtc aaa tgc	816
	Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser	
	260 265 270	
45	ttt gtg cag aag gtc tgt aat gaa cag ctg acc cac tgg ttt gaa gcc	864
	Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala	
	275 280 285	
50	aac ccc acc gac tgc aaa gtc gtt gtg aac aag gct gtg tcc tgc gcg	912
	Asn Pro Thr Asp Ser Lys Val Val Val Asn Lys Ala Val Ser Ser Ala	
	290 295 300	
55	caa gcc cgt atc gcg gca cgt aag gca cga gag ttg gtg cgg cgt aag	960
	Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys	
	305 310 315 320	
60	agc gcc acc gac atc ggt gga ttg ccc ggc aag ctg gcc gat tgc cgt	1008
	Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg	
	325 330 335	
65	tcc acg gat ccg cgc aag tcc gaa ctg tat gtc gta gaa ggt gac tgc	1056
	Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser	
	340 345 350	

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 ctt ccg ctg cgc ggc aag atc atc aat gtg gag aaa gcg cgc atc gac 1152
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 370 375 380
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 cgg gtg cta aag aac acc gaa gtt cag gcg atc atc acg gcg ctg gcc 1200
 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
 385 390 395 400
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 Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp
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 Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
 65 70 75 80
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 Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
 85 90 95
 Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val
 100 105 110
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 Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala
 115 120 125
 Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro
 130 135 140
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 Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
 145 150 155 160

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Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu
165 170 175
5 Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
180 185 190
Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
195 200 205
10 Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
210 215 220
Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
225 230 235 240
15 Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
245 250 255
Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
260 265 270
20 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
275 280 285
Asn Pro Thr Asp Ser Lys Val Val Val Asn Lys Ala Val Ser Ser Ala
290 295 300
25 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
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30 Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
325 330 335
Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
340 345 350
35 Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
355 360 365
Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
370 375 380
40 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
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45 Ile Val Leu

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 Gly Glu Asn Ser Gly Tyr Asn Val Ser Gly Gly Leu His Gly Val Gly
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 gtg tcg gtg gtg aac gcg ctg tcg acc cgg ctc gag gtc gac atc aag 96
 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Ile Lys
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 cgt gac ggc cac aag tgg tcg cag ttc tac aac aag gcc gtg ccg ggc 144
 Arg Asp Gly His Lys Trp Ser Gln Phe Tyr Asn Lys Ala Val Pro Gly
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 Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
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 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 Thr Ile Asn Leu Thr Asp Glu Arg Val Ala Gln Asp Glu Val Val Asp
 100 105 110
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 Glu Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Glu Glu Lys
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 gtg cac acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac 624

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	Glu	Glu	Gly	Phe	Arg	Ser	Ala	Leu	Thr	Ser	Val	Val	Asn	Lys	Tyr	Ala	
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	Lys	Asp	Lys	Lys	Leu	Leu	Lys	Glu	Lys	Asp	Ala	Asn	Leu	Thr	Gly	Asp	
	225					230					235					240	
15	gac	att	cgc	gag	ggc	ctg	gcc	gag	gtc	atc	tcg	gtg	aaa	gtt	gcc	gaa	768
	Asp	Ile	Arg	Glu	Gly	Leu	Ala	Ala	Val	Ile	Ser	Val	Lys	Val	Ala	Glu	
					245					250					255		
20	ccg	cag	ttc	gag	ggc	cag	acc	aag	acc	aaa	ctg	ggt	aac	acc	gag	gtc	816
	Pro	Gln	Phe	Glu	Gly	Gln	Thr	Lys	Thr	Lys	Leu	Gly	Asn	Thr	Glu	Val	
				260					265					270			
25	aag	tcg	ttc	gta	cag	aag	gtc	tgc	aac	gaa	cag	ctg	acc	cac	tgg	ttc	864
	Lys	Ser	Phe	Val	Gln	Lys	Val	Cys	Asn	Glu	Gln	Leu	Thr	His	Trp	Phe	
			275					280					285				
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	Glu	Ala	Asn	Pro	Ser	Glu	Ala	Lys	Thr	Val	Val	Asn	Lys	Ala	Val	Ser	
	290						295					300					
35	tcg	gca	cag	gcg	cgt	atc	gcc	gcc	cgc	aag	gca	cga	gag	ttg	gtg	cgt	960
	Ser	Ala	Gln	Ala	Arg	Ile	Ala	Ala	Arg	Lys	Ala	Arg	Glu	Leu	Val	Arg	
	305					310					315					320	
40	cgc	aag	agc	gct	acc	gat	ctc	ggt	ggg	ctg	ccc	ggc	aag	ctg	gcc	gac	1008
	Arg	Lys	Ser	Ala	Thr	Asp	Leu	Gly	Gly	Leu	Pro	Gly	Lys	Leu	Ala	Asp	
					325					330					335		
45	tgc	cgc	tcc	acc	gat	ccg	cgc	aag	tcg	gaa	ttg	tat	gtg	gtg	gaa	ggg	1056
	Cys	Arg	Ser	Thr	Asp	Pro	Arg	Lys	Ser	Glu	Leu	Tyr	Val	Val	Glu	Gly	
				340					345					350			
50	gac	tcg	gcc	ggc	ggc	tcc	gcc	aag	agc	ggc	cgc	gac	tcg	atg	ttt	cag	1104
	Asp	Ser	Ala	Gly	Gly	Ser	Ala	Lys	Ser	Gly	Arg	Asp	Ser	Met	Phe	Gln	
			355					360					365				
55	gcg	ata	ctt	ccg	ttg	cgc	ggc	aag	atc	atc	aac	gtc	gag	aag	gcc	cgc	1152
	Ala	Ile	Leu	Pro	Leu	Arg	Gly	Lys	Ile	Ile	Asn	Val	Glu	Lys	Ala	Arg	
	370						375					380					
60	atc	gac	cgg	gtg	ctg	aag	aac	acc	gaa	gtc	cag	gcg	atc	atc	acc	gcg	1200
	Ile	Asp	Arg	Val	Leu	Lys	Asn	Thr	Glu	Val	Gln	Ala	Ile	Ile	Thr	Ala	
	385					390					395					400	
65	ctg	ggt	acc	gga	att	cac	gac	gag	ttc	gac	ctc	gcc	aaa	ctg	cgc	tac	1248
	Leu	Gly	Thr	Gly	Ile	His	Asp	Glu	Phe	Asp	Leu	Ala	Lys	Leu	Arg	Tyr	
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His Lys Ile Val Leu
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Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
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Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
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Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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Thr Ile Asn Leu Thr Asp Glu Arg Val Ala Gln Asp Glu Val Val Asp
100 105 110

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Glu Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Glu Glu Lys
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Ala Ala Glu Ser Lys Gly Pro His Lys Val Lys His Arg Thr Phe His
130 135 140

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Tyr Pro Gly Gly Leu Ile Asp Phe Val Lys His Ile Asn Arg Thr Lys
145 150 155 160

Ser Pro Ile Gln Gln Ser Val Val Ala Phe Asp Gly Lys Gly Glu Gly
165 170 175

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His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
180 185 190

Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
195 200 205

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Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
210 215 220

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Lys Asp Lys Lys Leu Leu Lys Glu Lys Asp Ala Asn Leu Thr Gly Asp
225 230 235 240

Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu

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245 250 255
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 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
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 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
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 20 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
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 370 375 380
 25 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Val Ala
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 Arg Asp Gly Tyr Met Trp Ser Gln Phe Tyr Asp His Ala Glu Pro Gly
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15	acg gtg gcg cgc cga ctg cag gaa atg gcg ttc ctg aac aag ggt ttg Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu 85 90 95	288		
20	acg atc aac ctc acc gac gag cgg gtc agt gaa gag gag gtc gtc gac Thr Ile Asn Leu Thr Asp Glu Arg Val Ser Glu Glu Glu Val Val Asp 100 105 110	336		
25	gat gtc gtc agc gac acc gcc gag gca ccc aag tcc gcc gta gaa aaa Asp Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Val Glu Lys 115 120 125	384		
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45	cac gag gtc gaa atc gcg atg cag tgg aat gcc ggc tac tcg gag tcg His Glu Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser 180 185 190	576		
50	gtg cac acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His 195 200 205	624		
55	gaa gag ggc ttc cgc agc gcg ttg acg tcg gtg gtc aac aaa tac gcc Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala 210 215 220	672		
60	aag gac cgc aaa ctc ctg aag gac aaa gac ccc aac ctc acc ggc gac Lys Asp Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp 225 230 235 240	720		
65	gac atc cgg gaa ggc ctg gca gcg gtc att tcc gtc aag gtc agc gaa Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu 245 250 255	768		
70	ccg caa ttc gag ggc cag acc aaa acc aag ctg ggc aac acc gag gtc Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val	816		

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15	tgc gcc cag gcc cga atc gca gcg cgc aag gcg cga gaa ctg gtg cgc Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg 305 310 315 320			960
20	cgc aag agc gcc acc gac ctc ggt ggc ctg ccg ggt aag ctc gca gac Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp 325 330 335			1008
25	tgc cgc tcc acc gac ccg cga aag tgc gaa ctg tat gtg gtg gag ggt Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly 340 345 350			1056
30	gac tgc gcc ggc ggc tgc gcc aag agc ggc cgc gac tgc atg ttc cag Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln 355 360 365			1104
35	gcg atc ctc ccg ctg cgt ggc aag atc atc aac gtc gag aag gcg cgc Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg 370 375 380			1152
40	atc gac cgg gtg ctg aag aac acc gaa gtt cag gcg atc atc acc gcg Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala 385 390 395 400			1200
45	ctg ggc acg ggc att cac gac gag ttc gac atc acc aag ctc cgg tac Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr 405 410 415			1248
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	35	40	45
5	Thr Leu Lys Gln Gly Glu Ala Thr Lys Thr Thr Gly Thr Thr Ile Arg 50 55 60		
	Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu 65 70 75 80		
10	Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu 85 90 95		
	Thr Ile Asn Leu Thr Asp Glu Arg Val Ser Glu Glu Glu Val Val Asp 100 105 110		
15	Asp Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Val Glu Lys 115 120 125		
	Ala Ala Glu Ser Thr Gly Pro His Lys Val Lys His Arg Thr Phe His 130 135 140		
20	Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys 145 150 155 160		
	Asn Pro Ile His Asn Ser Ile Val Asp Phe Ser Gly Lys Gly Pro Gly 165 170 175		
25	His Glu Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser 180 185 190		
	Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His 195 200 205		
30	Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala 210 215 220		
	Lys Asp Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp 225 230 235 240		
	Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu 245 250 255		
40	Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val 260 265 270		
	Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe 275 280 285		
45	Glu Ala Asn Pro Ala Asp Ala Lys Thr Val Val Asn Lys Ala Val Ser 290 295 300		
	Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg 305 310 315 320		
50	Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp 325 330 335		

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Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
 5 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
 10 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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 30 gtc tcg gtg gtc aac gcg ctg tcg acc cgg ctc gag gtg gac atc gcc 96
 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Ile Ala
 20 25 30
 35 cgc gat ggc tac gaa tgg tcg cag ttc tac gac cac gcc gta ccc gga 144
 Arg Asp Gly Tyr Glu Trp Ser Gln Phe Tyr Asp His Ala Val Pro Gly
 35 40 45
 40 acg ctc aaa cag ggt gag gcc acc aag cgg acg ggc acc acg atc agg 192
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg
 50 55 60
 45 ttc tgg gcc gac ccc gac atc ttc gag acc acc gag tac gac ttc gag 240
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
 65 70 75 80
 acg gtg gcg cgc cgg ctg cag gaa atg gcg ttc ctc aac aag ggg ttg 288
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
 85 90 95
 50 acc atc aac ctc acc gac gag cgg gtg agc aac gag gag gtc gtc gac 336
 Thr Ile Asn Leu Thr Asp Glu Arg Val Ser Asn Glu Glu Val Val Asp
 100 105 110
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5	gag gtc gtc agc gat acc gcc gac gca ccc aag tgc gcc cag gaa aag Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys 115 120 125	384
10	gcg gcg gaa tgc act gcg cca cat aag gtt aag cac cgc acc ttc cac Ala Ala Glu Ser Thr Ala Pro His Lys Val Lys His Arg Thr Phe His 130 135 140	432
15	tac ccc ggc ggt ctg gtc gac ttc gtc aag cac atc aac cgc acc aag Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys 145 150 155 160	480
20	agc ccg atc cag cag agc atc atc gac ttc gac ggc aaa ggt ccc ggc Ser Pro Ile Gln Gln Ser Ile Ile Asp Phe Asp Gly Lys Gly Pro Gly 165 170 175	528
25	cac gag gtc gag atc gcg atg cag tgg aac ggc ggc tac tgc gaa tcc His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser 180 185 190	576
30	gtg cac acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His 195 200 205	624
35	gaa gag ggc ttc cgc agc gcg ctg acg tgc gtg gtg aac aag tac gcc Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala 210 215 220	672
40	aaa gac aag aag ttg ctg aaa gac aag gac ccg aac ctc acc ggc gac Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp 225 230 235 240	720
45	gac att cgc gaa ggc ctg gcc gcg gtg atc tgc gtc aag gtc agc gaa Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu 245 250 255	768
50	ccg cag ttc gag ggt cag acc aag acc aag ctg ggc aac acc gaa gtg Pro Gln Phe Glu Gly Gln Thr Lys Lys Leu Gly Asn Thr Glu Val 260 265 270	816
55	aag tgc ttc gtg cag aag gtc tgc aac gaa cag ctc acc cac tgg ttc Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe 275 280 285	864
60	gag gcc aac ccc gcg gac gcc aag gtg gtg gtc aac aag gcg gtg tgc Glu Ala Asn Pro Ala Asp Ala Lys Val Val Val Asn Lys Ala Val Ser 290 295 300	912
65	tgc gcg cag gcc cgg atc gcc gcg cgc aag gcg cga gag ttg gtg cgt Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg 305 310 315 320	960
70	cgc aag agc gcc acc gat ctg ggc ggg ctg ccc ggc aag ctc gcc gac Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp 325 330 335	1008

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tgc cgc tcg acg gat ccg cgc aag tgc gaa ctg tat gtg gtg gag ggt 1056
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 355 360 365
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 gcc atc ctg ccg ctg cgc ggc aag atc atc aac gtc gag aag gcc cgc 1152
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
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 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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 ctg ggc acc ggc atc cac gac gag ttc gac atc acc aag ctg cgc tat 1248
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 cac aag atc gtg ctg 1263
 His Lys Ile Val Leu
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 Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg
 50 55 60
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
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 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 Thr Ile Asn Leu Thr Asp Glu Arg Val Ser Asn Glu Glu Val Val Asp
 100 105 110
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 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys
 115 120 125
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Ala Ala Glu Ser Thr Ala Pro His Lys Val Lys His Arg Thr Phe His
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5 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
145 150 155 160

Ser Pro Ile Gln Gln Ser Ile Ile Asp Phe Asp Gly Lys Gly Pro Gly
165 170 175

10 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
180 185 190

Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
195 200 205

15 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
210 215 220

Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
225 230 235 240

20 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu
245 250 255

Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
260 265 270

25 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
275 280 285

Glu Ala Asn Pro Ala Asp Ala Lys Val Val Val Asn Lys Ala Val Ser
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30 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
305 310 315 320

35 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
325 330 335

Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
340 345 350

40 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
355 360 365

Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
370 375 380

45 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr
405 410 415

50 His Lys Ile Val Leu
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 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asn Ile Ala
 20 25 30
 cgc gac ggc tac gag tgg tgg cag tac tac gac cac gcc gtg ccc ggc 144
 Arg Asp Gly Tyr Glu Trp Ser Gln Tyr Tyr Asp His Ala Val Pro Gly
 35 40 45
 acc ctc aag cag ggc gag gcc acc aag cgc acc ggc acc acc atc cgg 192
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg
 50 55 60
 ttc tgg gcc gac ccc gac atc ttc gag acc acc gag tac gac ttc gaa 240
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
 65 70 75 80
 acg gtg gcc cgg cgg ctg cag gaa atg gcg ttc ctc aac aag ggc ctg 288
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 Thr Ile Asn Leu Thr Asp Glu Arg Val Thr Asn Glu Glu Val Val Asp
 100 105 110
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 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys
 115 120 125
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 Ala Ala Glu Ser Ala Ala Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140
 tac ccc ggc ggc ctg gtc gac ttc gtc aaa cac atc aat cgc acc aaa 480
 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160
 aac ccc atc cac cag agc atc atc gat ttc ggt ggg aag ggc ccc ggc 528
 Asn Pro Ile His Gln Ser Ile Ile Asp Phe Gly Gly Lys Gly Pro Gly
 165 170 175

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 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
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 gtg cac acc ttc gcc aac acc atc aac acg cac gag ggc ggc acc cac 624
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
 195 200 205
 gag gag ggc ttc cgc agc gcg ctg acc tcc gtg gtc aac aag tac gcc 672
 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
 210 215 220
 aag gac aag aag ctg ctc aag gac aag gac ccc aac ctg acc ggc gac 720
 Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240
 gac atc cgc gag ggt ttg gcc gcg gtg atc tgg gtc aag gtg agc gaa 768
 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu
 245 250 255
 ccg cag ttc gag ggc cag acc aag acc aaa ctg ggc aac acc gag gtg 816
 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270
 aag tgg ttc gtg cag aag gtg tgc aac gaa cag ctc acc cac tgg ttc 864
 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
 275 280 285
 gaa gcc aac ccc gca gac gcc aaa gtc att gtc aac aag gcg gtt tca 912
 Glu Ala Asn Pro Ala Asp Ala Lys Val Ile Val Asn Lys Ala Val Ser
 290 295 300
 tca gcg cag gcg cgc atc gcc gcg cgc aag gcg cga gag ttg gtg cgc 960
 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320
 cgc aag agc gca acc gac ctg ggc ggc ctg ccc ggc aag ctc gcc gac 1008
 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335
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 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
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 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
 gcc atc ctt ccg ctg cgc ggc aag atc atc aac gtc gaa aag gcc cgc 1152
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
 atc gac cgg gtg ctg aag aac acc gag gtg cag gcg atc atc acc gcg 1200
 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
 385 390 395 400

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ctg ggc acc ggg att cac gac gag ttc gac atc acc aag ctg cgc tac 1248
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5 cac aag atc gtg ttg 1263
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Arg Asp Gly Tyr Glu Trp Ser Gln Tyr Tyr Asp His Ala Val Pro Gly 45
 35 40

Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg 60
 50 55

25 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu 80
 65 70 75

Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu 95
 85 90

30 Thr Ile Asn Leu Thr Asp Glu Arg Val Thr Asn Glu Glu Val Val Asp 110
 100 105

35 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys 125
 115 120

Ala Ala Glu Ser Ala Ala Pro His Lys Val Lys His Arg Thr Phe His 140
 130 135

40 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys 160
 145 150 155

Asn Pro Ile His Gln Ser Ile Ile Asp Phe Gly Gly Lys Gly Pro Gly 175
 165 170

45 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser 190
 180 185

Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His 205
 195 200

50 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala 220
 210 215

55

Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240
 5 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu
 245 250 255
 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270
 10 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
 275 280 285
 Glu Ala Asn Pro Ala Asp Ala Lys Val Ile Val Asn Lys Ala Val Ser
 290 295 300
 15 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320
 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335
 20 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
 25 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
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 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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5	cgc	gac	ggg	cac	gag	tgg	tcg	cag	tat	tac	aag	cgc	gcg	gtg	ccg	ggc	144
	Arg	Asp	Gly	His	Glu	Trp	Ser	Gln	Tyr	Tyr	Lys	Arg	Ala	Val	Pro	Gly	
			35					40					45				
10	acc	ctc	aag	cag	ggt	gag	acg	acc	cgc	aag	acc	ggc	acc	aca	atc	cgg	192
	Thr	Leu	Lys	Gln	Gly	Glu	Thr	Thr	Arg	Lys	Thr	Gly	Thr	Thr	Ile	Arg	
			50				55					60					
15	ttc	tgg	gcg	gat	ccg	gag	atc	ttc	gag	acc	acc	caa	tac	gac	ttc	gag	240
	Phe	Trp	Ala	Asp	Pro	Glu	Ile	Phe	Glu	Thr	Thr	Gln	Tyr	Asp	Phe	Glu	
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20	acg	gtg	gcg	cgc	cgg	ctg	cag	gag	atg	gcg	ttc	ctg	aac	aag	ggt	ctg	288
	Thr	Val	Ala	Arg	Arg	Leu	Gln	Glu	Met	Ala	Phe	Leu	Asn	Lys	Gly	Leu	
				85					90						95		
25	acg	atc	aat	ctg	acc	gac	gaa	cgc	gtc	gag	cag	gac	gag	gtt	gtc	gac	336
	Thr	Ile	Asn	Leu	Thr	Asp	Glu	Arg	Val	Glu	Gln	Asp	Glu	Val	Val	Asp	
				100					105					110			
30	gag	gtc	gtc	agc	gac	acc	gcc	gaa	gcg	ccc	aaa	tcc	gcc	gaa	gag	aag	384
	Glu	Val	Val	Ser	Asp	Thr	Ala	Glu	Ala	Pro	Lys	Ser	Ala	Glu	Glu	Lys	
			115					120					125				
35	gct	gcc	gaa	toc	aag	gcc	ccg	cac	aag	gtc	aag	cag	cgc	acc	ttc	cac	432
	Ala	Ala	Glu	Ser	Lys	Ala	Pro	His	Lys	Val	Lys	Gln	Arg	Thr	Phe	His	
			130				135					140					
40	tat	ccc	ggt	ggt	ctg	gtc	gac	ttc	gtc	aaa	cac	atc	aac	cgc	acc	aaa	480
	Tyr	Pro	Gly	Gly	Leu	Val	Asp	Phe	Val	Lys	His	Ile	Asn	Arg	Thr	Lys	
	145				150						155					160	
45	agc	ccg	atc	cag	cag	agc	gtc	atc	gac	ttc	gaa	ggc	aaa	ggc	acc	ggc	528
	Ser	Pro	Ile	Gln	Gln	Ser	Val	Ile	Asp	Phe	Glu	Gly	Lys	Gly	Thr	Gly	
				165					170						175		
50	cac	gag	gtc	gaa	atc	gcg	atg	cag	tgg	aac	ggc	ggc	tac	tcc	gaa	tcg	576
	His	Glu	Val	Glu	Ile	Ala	Met	Gln	Trp	Asn	Gly	Gly	Tyr	Ser	Glu	Ser	
				180					185					190			
55	gtg	cac	acc	ttc	gcc	aac	acc	atc	aac	acc	cac	gag	ggc	ggc	acc	cac	624
	Val	His	Thr	Phe	Ala	Asn	Thr	Ile	Asn	Thr	His	Glu	Gly	Gly	Thr	His	
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	Glu	Glu	Gly	Phe	Arg	Ser	Ala	Leu	Thr	Ser	Val	Val	Asn	Lys	Tyr	Ala	
			210				215					220					
65	aaa	gac	aag	aag	ctg	ctc	aag	gag	aag	gac	ccg	aat	ctc	acc	ggt	gac	720
	Lys	Asp	Lys	Lys	Leu	Leu	Lys	Glu	Lys	Asp	Pro	Asn	Leu	Thr	Gly	Asp	
	225				230						235				240		
70	gac	atc	cgg	gag	ggg	ttg	gcc	gcg	gtg	atc	tcg	gtg	aag	gtc	gcc	gaa	768

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Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu
245 250 255

5 ccg cag ttc gag ggt cag acc aag acc aag ctg ggc aac acc gag gtc 816
Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
260 265 270

10 aag tcg ttc gtg cag aag gtg tgc aac gaa cag ctc acc cac tgg ttc 864
Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
275 280 285

gag gcc aat ccg tcg gaa gct aaa acc gtt gtg aac aaa gcg gtg tgc 912
Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser
290 295 300

15 tcc gcc cag gcg cgg atc gcc gcg cgc aaa gcg cga gag ctg gtg cgc 960
Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
305 310 315 320

20 cgc aag agc gca acc gac ctc ggc ggc ctg ccg ggc aag ctc gcc gac 1008
Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
325 330 335

25 tgc cgt tcg acg gat ccc cgc aaa tcc gaa ctg tat gtg gtg gag ggg 1056
Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
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gac tcc gcc ggc ggc tcg gcc aag agc ggt cgg gat tcg atg ttc cag 1104
Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
355 360 365

30 gcg att ctt ccg ttg cgc ggc aag atc atc aac gtc gag aag gcc cgc 1152
Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
370 375 380

35 atc gac cgg gtg ctg aag aac acc gaa gtc cag gcc atc atc acc gcg 1200
Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
385 390 395 400

ctg ggc acc ggg atc cac gac gag ttc gac atc acc aaa ctg cgc tac 1248
Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr
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His Lys Ile Val Leu
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EP 1 098 003 A2

Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Ile Lys
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5 Arg Asp Gly His Glu Trp Ser Gln Tyr Tyr Lys Arg Ala Val Pro Gly
35 40 45
Thr Leu Lys Gln Gly Glu Thr Thr Arg Lys Thr Gly Thr Thr Ile Arg
50 55 60
10 Phe Trp Ala Asp Pro Glu Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu
65 70 75 80
Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
85 90 95
15 Thr Ile Asn Leu Thr Asp Glu Arg Val Glu Gln Asp Glu Val Val Asp
100 105 110
Glu Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Glu Glu Lys
115 120 125
20 Ala Ala Glu Ser Lys Ala Pro His Lys Val Lys Gln Arg Thr Phe His
130 135 140
25 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
145 150 155 160
Ser Pro Ile Gln Gln Ser Val Ile Asp Phe Glu Gly Lys Gly Thr Gly
165 170 175
30 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
180 185 190
Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
195 200 205
35 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
210 215 220
Lys Asp Lys Lys Leu Leu Lys Glu Lys Asp Pro Asn Leu Thr Gly Asp
225 230 235 240
40 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu
245 250 255
Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
260 265 270
45 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
275 280 285
50 Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser
290 295 300
Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg

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305 310 315 320
 5 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335
 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
 10 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
 15 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
 385 390 395 400
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 405 410 415
 20 His Lys Ile Val Leu
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 35 gtg gtt aac gcg cta tcc acc cgg ctc gaa gtc gag atc aag cgc gac 96
 Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Glu Ile Lys Arg Asp
 20 25 30
 40 ggg tac gag tgg tct cag gtt tat gag aag tcg gaa ccc ctg ggc ctc 144
 Gly Tyr Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Leu Gly Leu
 35 40 45
 45 aag caa ggg gcg ccg acc aag aag acg ggg tca acg gtg cgg ttc tgg 192
 Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp
 50 55 60
 gcc gac ccc gct gtt ttc gaa acc acg gaa tac gac ttc gaa acc gtc 240
 Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
 65 70 75 80
 50 gcc cgc cgg ctg caa gag atg gcg ttc ctc aac aag ggg ctg acc atc 288
 Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
 55

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	85	90	95	
5	aac ctg acc gac gag agg gtg acc caa gac gag gtc gtc gac gaa gtg Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val 100 105 110			336
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15	gaa tcc act gca ccg cac aaa gtt aag agc cgc acc ttt cac tat ccg Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro 130 135 140			432
20	ggt ggc ctg gtg gac ttc gtg aaa cac atc aac cgc acc aag aac gcg Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala 145 150 155 160			480
25	att cat agc agc atc gtg gac ttt tcc ggc aag ggc acc ggg cac gag Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu 165 170 175			528
30	gtg gag atc gcg atg caa tgg aac gcc ggg tat tgc gag tgc gtg cac Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His 180 185 190			576
35	acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac gaa gag Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu 195 200 205			624
40	ggc ttc cgc agc gcg ctg acg tgc gtg gtg aac aag tac gcc aag gac Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp 210 215 220			672
45	cgc aag cta ctg aag gac aag gac ccc aac ctc acc ggt gac gat atc Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile 225 230 235 240			720
50	cgg gaa ggc ctg gcc gct gtg atc tgc gtg aag gtc agc gaa ccg cag Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln 245 250 255			768
55	ttc gag ggc cag acc aag acc aag ttg ggc aac acc gag gtc aaa tgc Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser 260 265 270			816
60	ttt gtg cag aag gtc tgt aac gaa cag ctg acc cac tgg ttt gaa gcc Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala 275 280 285			864
65	aac ccc acc gac tgc aaa gtc gtt gtg aac aag gct gtg tcc tgc gcg Asn Pro Thr Asp Ser Lys Val Val Val Asn Lys Ala Val Ser Ser Ala 290 295 300			912
70	caa gcc cgt atc gcg gca cgt aag gca cga gag ttg gtg cgg cgt aag Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys 305 310 315			960

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	305		310		315		320	
5	agc gcc acc gac atc ggt gga ttg ccc ggc aag ctg gcc gat tgc cgt							1008
	Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg							
		325			330		335	
10	tcc acg gat ccg cgc aag tcc gaa ctg tat gtc gta gaa ggt gac tcg							1056
	Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser							
		340			345		350	
15	gcc ggc ggt tct gca aaa agc ggt cgc gat tcg atg ttc cag gcg ata							1104
	Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile							
		355			360		365	
20	ctt ccg ctg cgc ggc aag atc atc aat gtg gag aaa gcg cgc atc gac							1152
	Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp							
		370			375		380	
25	cgg gtg cta aag aac acc gaa gtt cag gcg atc atc acg gcg ctg ggc							1200
	Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly							
		385			390		395	400
30	acc ggg atc cac gac gag ttc gat atc ggc aag ctg cgc tac cac aag							1248
	Thr Gly Ile His Asp Glu Phe Asp Ile Gly Lys Leu Arg Tyr His Lys							
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35	atc gtg ctg							1257
	Ile Val Leu							
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	20 25 30							
55	Gly Tyr Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Leu Gly Leu							
	35 40 45							
60	Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp							
	50 55 60							
65	Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val							
	65 70 75 80							
70	Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile							
	85 90 95							
75	Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val							
	100 105 110							

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Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala
115 120 125

5 Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro
130 135 140

Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
145 150 155 160

10 Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu
165 170 175

Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
180 185 190

15 Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
195 200 205

Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
210 215 220

20 Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
225 230 235 240

Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
245 250 255

25 Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
260 265 270

30 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
275 280 285

Asn Pro Thr Asp Ser Lys Val Val Val Asn Lys Ala Val Ser Ser Ala
290 295 300

35 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
305 310 315 320

Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
325 330 335

40 Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
340 345 350

Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
355 360 365

45 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
370 375 380

Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
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405 410 415

Ile Val Leu

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Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Glu Ile Lys Arg Asp	
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ggg tac gag tgg tct cag gtt tat gag aag tcg gaa ccc ctg ggc ctc	144
Gly Tyr Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Leu Gly Leu	
35 40 45	
aag caa ggg gcg ccg acc aag aag acg ggg tca acg gtg cgg ttc tgg	192
Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp	
50 55 60	
gcc gac ccc gct gtt ttc gaa acc acg gaa tac gac ttc gaa acc gtc	240
Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val	
65 70 75 80	
gcc cgc cgg ctg caa gag atg gcg ttc ctc aac aag ggg ctg acc atc	288
Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile	
85 90 95	
aac ctg acc gac gag agg gtg acc caa gac gag gtc gtc gac gaa gtg	336
Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val	
100 105 110	
gtc agc gac gtc gcc gag gcg ccg aag tcg gca agt gaa cgc gca gcc	384
Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala	
115 120 125	
gaa tcc act gca ccg cac aaa gtt aag agc cgc acc ttt cac tat ccg	432
Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro	
130 135 140	
ggt ggc ctg gtg gac ttc gtg aaa cac atc aac cgc acc aag aac gcg	480
Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala	
145 150 155 160	

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 165 170 175

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 gtg gag atc gcg atg caa tgg aac gcc ggg tat tcg gag tcg gtg cac 576
 Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
 180 185 190

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 acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac gaa gag 624
 Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
 195 200 205

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 ggc ttc cgc agc gcg ctg acg tcg gtg gtg aac aag tac gcc aag gac 672
 Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
 210 215 220

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 cgc aag cta ctg aag gac aag gac ccc aac ctc acc ggt gac gat atc 720
 Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
 225 230 235 240

25
 cgg gaa ggc ctg gcc gct gtg atc tcg gtg aag gtc agc gaa ccg cag 768
 Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
 245 250 255

30
 ttc gag ggc cag acc aag acc aag ttg ggc aac acc gag gtc aaa tcg 816
 Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
 260 265 270

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 ttt gtg cag aag gtc tgt aac gaa cag ctg acc cac tgg ttt gaa gcc 864
 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
 275 280 285

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 aac ccc acc gac gcg aaa gtc gtt gtg aac aag gct gtg tcc tcg gcg 912
 Asn Pro Thr Asp Ala Lys Val Val Val Asn Lys Ala Val Ser Ser Ala
 290 295 300

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 caa gcc cgt atc gcg gca cgt aag gca cga gag ttg gtg cgg cgt aag 960
 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
 305 310 315 320

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 agc gcc acc gac atc ggt gga ttg ccc ggc aag ctg gcc gat tgc cgt 1008
 Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
 325 330 335

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 tcc acg gat ccg cgc aag tcc gaa ctg tat gtc gta gaa ggt gac tcg 1056
 Ser Thr Asp Pro Arg Lys Ser Glu Tyr Val Val Glu Gly Asp Ser
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 Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
 355 360 365

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 ctt ccg ctg cgc ggc aag atc atc aat gtg gag aaa gcg cgc atc gac 1152
 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
 370 375 380

EP 1 098 003 A2

5 cgg gtg cta aag aac acc gaa gtt cag gcg atc atc acg gcg ctg ggc 1200
 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
 385 390 395 400

acc ggg atc cac gac gag ttc gat atc ggc aag ctg cgc tac cac aag 1248
 Thr Gly Ile His Asp Glu Phe Asp Ile Gly Lys Leu Arg Tyr His Lys
 405 410 415

10 atc gtg ctg 1257
 Ile Val Leu

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 35 40 45

Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp
 50 55 60

30 Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
 65 70 75 80

Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
 85 90 95

35 Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val
 100 105 110

Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala
 115 120 125

40 Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro
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Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
 145 150 155 160

45 Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu
 165 170 175

Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
 180 185 190

50 Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
 195 200 205

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Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
 210 215 220
 5 Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
 225 230 235 240
 Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
 245 250 255
 10 Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
 260 265 270
 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
 275 280 285
 15 Asn Pro Thr Asp Ala Lys Val Val Val Asn Lys Ala Val Ser Ser Ala
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 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
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 20 Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
 325 330 335
 Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
 340 345 350
 25 Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
 355 360 365
 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
 370 375 380
 30 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
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48

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5	gtg gtc aac gcg ctg tcc atc cgg ctg gag gtg gag atc aag cgc gac	Val Val Asn Ala Leu Ser Ile Arg Leu Glu Val Glu Ile Lys Arg Asp	96		
		20	25	30	
10	ggc cat gag tgg tcg caa gtt tat gag aag tcc gag ccg atg gga ctc	Gly His Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Met Gly Leu	144		
		35	40	45	
15	aag caa ggc gcg ccg acg aag aag acc ggc acg acg gtg ccg ttc tgg	Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Thr Val Arg Phe Trp	192		
		50	55	60	
20	gcc gac ccc aac gtt ttt gaa acc acc gag tac gac ttc gaa acc gtc	Ala Asp Pro Asn Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val	240		
		65	70	75	80
25	gcg cga cgg ttg cag gag atg gcg ttt ctc aac aag ggg ctc acc atc	Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile	288		
		85	90	95	
30	aac ctg acc gat cag cgg gta acc cag gac gaa gtg gtc gac gag gtg	Asn Leu Thr Asp Gln Arg Val Thr Gln Asp Glu Val Val Asp Glu Val	336		
		100	105	110	
35	gtc agc gac gtc gcc gag gcc ccg aag tcg gcc agt gag aag gcg gcc	Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Lys Ala Ala	384		
		115	120	125	
40	gaa ttc acc gcc ccc cac aag gtg aag aag cgt acc ttt cac tat ccc	Glu Phe Thr Ala Pro His Lys Val Lys Lys Arg Thr Phe His Tyr Pro	432		
		130	135	140	
45	ggg ggc ttg gtt gac ttc gtc aag cac atc aac cgc acc aag aac gcc	Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala	480		
		145	150	155	160
50	atc cac agc agc atc gtc gac ttc tcc gga aag ggg acc ggc cac gaa	Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu	528		
		165	170	175	
55	gtg gag atc gcg atg cag tgg aat gcc ggc tat tcg gag tcg gtg cac	Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His	576		
		180	185	190	
60	acc ttc gcc aac acc atc aac acc cat gag ggc ggg acc cat gaa gaa	Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu	624		
		195	200	205	
65	ggg ttc cgc agc gcg ctc acg tcc gtg gtg aac aag tac gcc aag gac	Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp	672		
		210	215	220	
70	cgc aaa ctg ctc aaa gac aag gac ccc aac ctc acc ggc gac gac atc	Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile	720		

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10	ttc gag ggc cag acc aag acg aaa cta ggc aac acc gag gtg aag tgc				816
	Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser				
		260	265	270	
15	ttc gtg cag aag gtg tgc aat gaa cag ctc acc cat tgg ttc gag gcc				864
	Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala				
		275	280	285	
20	aac ccc gct gat gct aaa acc gtt gtc aac aag gca gtt tca tgc gcg				912
	Asn Pro Ala Asp Ala Lys Thr Val Val Asn Lys Ala Val Ser Ser Ala				
		290	295	300	
25	cag gcc agg att gcg gcc cgc aag gcg cgc gag ttg gtg cgc cgc aag				960
	Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys				
		305	310	315	320
30	agc gca acc gat ctg gcg gga cta ccg ggc aag ttg gcc gac tgc cgc				1008
	Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg				
		325	330	335	
35	tcg acc gac ccc cgt aag tcc gaa tta tat gtg gtg gag ggt gat tca				1056
	Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser				
		340	345	350	
40	gcc ggc ggc tgc gcg aag agc ggc cgc gac tgc atg ttt caa gcg atc				1104
	Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile				
		355	360	365	
45	ttg ccg ttg cgc ggc aag atc atc aac gtc gag aag gcc cgc atc gac				1152
	Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp				
		370	375	380	
50	cgg gtg ctg aag aac acc gaa gtc cag gcg atc atc acc gcg ttg ggc				1200
	Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly				
		385	390	395	400
55	acc ggt att cac gac gaa ttc gac atc gcg aga ctg cgt tac cac aag				1248
	Thr Gly Ile His Asp Glu Phe Asp Ile Ala Arg Leu Arg Tyr His Lys				
		405	410	415	
60	atc gtg ctg				1257
	Ile Val Leu				
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70	<400> 26				

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 Val Val Asn Ala Leu Ser Ile Arg Leu Glu Val Glu Ile Lys Arg Asp
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 35 40 45
 Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Thr Thr Val Arg Phe Trp
 50 55 60
 Ala Asp Pro Asn Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
 65 70 75 80
 Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
 85 90 95
 Asn Leu Thr Asp Gln Arg Val Thr Gln Asp Glu Val Val Asp Glu Val
 100 105 110
 Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Lys Ala Ala
 115 120 125
 Glu Phe Thr Ala Pro His Lys Val Lys Lys Arg Thr Phe His Tyr Pro
 130 135 140
 Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
 145 150 155 160
 Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu
 165 170 175
 Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
 180 185 190
 Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
 195 200 205
 Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
 210 215 220
 Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
 225 230 235 240
 Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
 245 250 255
 Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
 260 265 270
 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
 275 280 285
 Asn Pro Ala Asp Ala Lys Thr Val Val Asn Lys Ala Val Ser Ser Ala
 290 295 300

Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
 305 310 315 320
 5 Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
 325 330 335
 Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
 340 345 350
 10 Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
 355 360 365
 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
 370 375 380
 15 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
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 20 Ile Val Leu
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 40 gtg tcg gtg gtc aac gcg ctg tcc acc cga ctg gaa gtc gac atc aag 96
 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Ile Lys
 20 25 30
 45 cgc gac gga tac gag tgg tcg cag ttc tac gac cgc gcc cag ccg ggc 144
 Arg Asp Gly Tyr Glu Trp Ser Gln Phe Tyr Asp Arg Ala Gln Pro Gly
 35 40 45
 acc ctc aaa cag ggc gag gca acc aag aag acc gga acc acc atc cgg 192
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
 50 55 60
 50 ttc tgg gcc gac tcg gac atc ttt gag acc acc gaa tac gac ttc gag 240
 Phe Trp Ala Asp Ser Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
 65 70 75 80
 55

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acg gtg gcg cgg cgc ctg cag gag atg gcg ttc ctc aac aag ggc ctg 288
Thr Val Ala Arg Arg 85 Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu 95

acc atc aac ctc acc gac gag cgg gtc acc ccg gac gag gtc gtc gac 336
Thr Ile Asn 100 Leu Thr Asp Glu Arg Val 105 Thr Pro Asp Glu Val 110 Val Asp

gac gtc gtc agt gat acc gcc gaa gca cca aag tcc gcc cag gag aag 384
Asp Val 115 Val Ser Asp Thr Ala Glu 120 Ala Pro Lys Ser Ala Gln Glu Lys 125

gcc gcc gaa tcg acc gcg ccg cac aag gtc aag agc cgc acc ttc cac 432
Ala Ala Glu 130 Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His 140

tat ccc ggc ggt ttg gtc gat ttc gtc aag cac atc aac cgc acc aag 480
Tyr Pro Gly Gly Leu Val 150 Asp Phe Val Lys His Ile Asn Arg Thr Lys 160

agt ccg att cag cag agc atc gtc gac ttc gag ggc aag ggc tcc gcc 528
Ser Pro Ile Gln Gln Ser Ile Val Asp Phe Glu Gly Lys Gly Ser Gly 175

cac gaa gtc gaa atc gcg atg cag tgg aac ggc ggc tac tcg gag tcg 576
His Glu Val 180 Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser 190

gtg cac acc ttc gcc aac acc atc aac acc cat gag ggt gga acg cac 624
Val His 195 Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His 205

gaa gag ggc ttc cgc agt gcg ttg acc tcg gtg gtg aac aag tac gcc 672
Glu Glu Gly Phe Arg Ser 210 Glu Leu Thr Ser Val 220 Val Asn Lys Tyr Ala

aaa gac aag aag ctg ctc aag gac aag gac ccc aac ctc acc ggt gac 720
Lys Asp Lys Lys Leu 230 Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp 240

gac atc cgc gag ggg ttg gcc gcg gtc atc tcg gtg cgg gtg gca gag 768
Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Arg Val Ala Glu 255

ccg cag ttc gag ggt cag acg aag acc aag ctg ggc aac acc gag gtc 816
Pro Gln Phe Glu Gly Gln Thr Lys Thr 265 Lys Leu Gly Asn Thr Glu Val 270

aag tcg ttt gtc cag aag gtt tgt aac gag cag ctc acc cac tgg ttc 864
Lys Ser 275 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe 285

gag gcc aat cct tcg gaa gcc aaa acc att gtg aac aag gcg gta tcc 912
Glu Ala Asn Pro Ser Glu Ala Lys Thr Ile Val Asn Lys Ala Val Ser 300

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	tcg gcg cag gca cgt ctc gcc gcg cgc aag cgc cga gag ttg gtg cgt	960
	Ser Ala Gln Ala Arg Leu Ala Ala Arg Lys Ala Arg Glu Leu Val Arg	
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5	cgc aag agc gca acc gat ctc ggt ggg ctg ccc ggc aag ttg gcc gac	1008
	Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp	
	325 330 335	
10	tgc cgc tcg aca gat ccg cgt aag tcg gaa ctg tat gtg gtg gag ggt	1056
	Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly	
	340 345 350	
15	gac tcg gcc ggc ggc tcg gca aag agt ggc cgc gat tcg atg ttc cag	1104
	Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln	
	355 360 365	
	gcg atc ctg ccg ctg cgc ggc aag atc atc aat gtc gaa aag gca cgc	1152
	Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg	
	370 375 380	
20	atc gac cga gtc ctg aaa aac act gaa gtc cag gcg atc atc acc gcg	1200
	Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala	
	385 390 395 400	
25	ttg ggt acc ggt att cac gac gaa ttc gac ctc tcg aag ctg cgc tat	1248
	Leu Gly Thr Gly Ile His Asp Glu Phe Asp Leu Ser Lys Leu Arg Tyr	
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	cac aag atc gtc ttg	1263
	His Lys Ile Val Leu	
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	20 25 30	
	Arg Asp Gly Tyr Glu Trp Ser Gln Phe Tyr Asp Arg Ala Gln Pro Gly	
	35 40 45	
45	Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg	
	50 55 60	
	Phe Trp Ala Asp Ser Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu	
	65 70 75 80	
50	Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu	
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Thr Ile Asn Leu Thr Asp Glu Arg Val Thr Pro Asp Glu Val Val Asp
100 105 110

5 Asp Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Gln Glu Lys
115 120 125

Ala Ala Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His
130 135 140

10 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
145 150 155 160

Ser Pro Ile Gln Gln Ser Ile Val Asp Phe Glu Gly Lys Gly Ser Gly
165 170 175

15 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
180 185 190

Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
195 200 205

20 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
210 215 220

Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
225 230 235 240

Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Arg Val Ala Glu
245 250 255

30 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
260 265 270

Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
275 280 285

35 Glu Ala Asn Pro Ser Glu Ala Lys Thr Ile Val Asn Lys Ala Val Ser
290 295 300

Ser Ala Gln Ala Arg Leu Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
305 310 315 320

40 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
325 330 335

Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
340 345 350

45 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
355 360 365

Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
370 375 380

50 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala

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	Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala	
	145 150 155 160	
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	165 170 175	
10	gtg gag atc gcg atg caa tgg aac gcc ggg tat tcg gag tcg gtg cac Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His	576
	180 185 190	
	acc ttc gcc aac acc atc aac acc cac gag ggc ggc acc cac gaa gag Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu	624
	195 200 205	
15	ggc ttc cgc agc gcg ctg acg tcg gtg gtg aac aag tac gcc aag gac Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp	672
	210 215 220	
20	cgc aag cta ctg aag gac aag gac ccc aac ctc acc ggt gac gat atc Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile	720
	225 230 235 240	
25	cgg gaa ggc ctg gcc gct gtg atc tcg gtg aag gtc agc gaa ccg cag Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln	768
	245 250 255	
	ttc gag ggc cag acc aag acc aag ttg ggc aac acc gag gtc aaa tcg Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser	816
	260 265 270	
30	ttt gtg cag aag gtc tgt aac gaa cag ctg acc cac tgg ttt gaa gcc Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala	864
	275 280 285	
35	aac ccc acc gac tcg aaa gtc gtt gtg aac aag gct gtg tcc tcg gcg Asn Pro Thr Asp Ser Lys Val Val Val Asn Lys Ala Val Ser Ser Ala	912
	290 295 300	
40	caa gcc cgt atc gcg gca cgt aag gca cga gag ttg gtg cgg cgt aag Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys	960
	305 310 315 320	
	agc gcc acc gac atc ggt gga ttg ccc ggc aag ctg gcc gat tgc cgt Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg	1008
	325 330 335	
45	tcc acg gat ccg cgc aag tcc gaa ctg tat gtc gta gaa ggt gac tcg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser	1056
	340 345 350	
50	gcc ggc ggt tct gca aaa agc ggt cgc gat tcg atg ttc cag gcg ata Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile	1104
	355 360 365	
55	ctt ccg ctg cgc ggc aag atc atc aat gtg gag aaa gcg cgc atc gac	1152

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Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
 370 375 380

5 cgg gtg cta aag aac acc gaa gtt cag gcg atc atc acg gcg ctg ggc 1200
 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
 385 390 395 400

10 acc ggg atc cac gac gag ttc gat atc ggc aag ctg cgc tac cac aag 1248
 Thr Gly Ile His Asp Glu Phe Asp Ile Gly Lys Leu Arg Tyr His Lys
 405 410 415

atc gtg ctg 1257
 Ile Val Leu

15 <210> 30
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Gly Tyr Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Leu Gly Leu
 35 40 45

30 Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Ser Thr Val Arg Phe Trp
 50 55 60

Ala Asp Pro Ala Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
 65 70 75 80

35 Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
 85 90 95

Asn Leu Thr Asp Glu Arg Val Thr Gln Asp Glu Val Val Asp Glu Val
 100 105 110

40 Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Arg Ala Ala
 115 120 125

Glu Ser Thr Ala Pro His Lys Val Lys Ser Arg Thr Phe His Tyr Pro
 130 135 140

45 Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
 145 150 155 160

Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Thr Gly His Glu
 165 170 175

50 Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val His
 180 185 190

55

Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
 195 200 205
 5 Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys Asp
 210 215 220
 Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp Ile
 225 230 235 240
 10 Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
 245 250 255
 Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys Ser
 15 260 265 270
 Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu Ala
 275 280 285
 Asn Pro Thr Asp Ser Lys Val Val Val Ash Lys Ala Val Ser Ser Ala
 20 290 295 300
 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
 305 310 315 320
 25 Ser Ala Thr Asp Ile Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
 325 330 335
 Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
 340 345 350
 30 Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
 355 360 365
 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
 370 375 380
 35 Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu Gly
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 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asp Ile Lys
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 10 cgc gac ggg cac gag tgg tcc cag tat tac gag cgc gcc gtt cct ggc 144
 Arg Asp Gly His Glu Trp Ser Gln Tyr Tyr Glu Arg Ala Val Pro Gly
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 15 acg ctc aag cag ggc gag gcg acc aag aag acc ggc acc acc atc cgg 192
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
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 20 ttc tgg gcg gac ccg gac atc ttc gag acc acc cag tac gac ttc gag 240
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu
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 acg gtg gcg cgc cgg ctc caa gag atg gcg ttc ctg aac aag ggc ttg 288
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 Thr Ile Asn Leu Thr Asp Glu Arg Val Asp Gln Asp Glu Val Val Asp
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 30 gaa gtc gtc agc gac acc gcc gat gcg ccc aag tcc gcc gaa gag aag 384
 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Glu Glu Lys
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 gcg gcc gaa tcc aaa gcg ccg cac aag gtt aag cac cgc acc ttc cac 432
 Ala Ala Glu Ser Lys Ala Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140
 35 tac ccc ggc ggc ttg gtc gac ttc gtc aag cac atc aac cgg acc aag 480
 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160
 40 agc ccg atc caa cag agc gtc atc gac ttc gag ggc aaa ggc acc ggc 528
 Ser Pro Ile Gln Gln Ser Val Ile Asp Phe Glu Gly Lys Gly Thr Gly
 165 170 175
 cac gag gtc gag atc gcg atg cag tgg aac ggt ggc tac tcg gag tcg 576
 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
 180 185 190
 45 gtg cac acc ttc gcc aac acg atc aac acc cac gag ggc ggt acg cac 624
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
 195 200 205
 50 gaa gaa ggg ttc cgc agt gcg ctg acg tcg gtg gtg aac aaa tac gcc 672
 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
 210 215 220

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 aaa gac aag aag ctg ctg aaa gac aag gac ccg aac ctc acc ggt gac 720
 Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240

10
 gac atc cgc gag gga ctg gcc gcg gtg atc tcg gtc aag gtc gcc gaa 768
 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu
 245 250 255

15
 ccc cag ttc gag ggc cag aca aag acc aag ctg ggc aac acc gag gtc 816
 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270

20
 aag tcg ttc gtg cag aag gtg tgc aac gaa cag ctc acc cac tgg ttc 864
 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
 275 280 285

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 gag gcc aat ccg tcg gaa gcc aaa acc gtt gtc aac aag gcg gtt tcg 912
 Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser
 290 295 300

30
 tcc gca cag gcc cgc atc gcg gcg cgg aag gcc cga gag ttg gtg cgg 960
 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320

35
 cgc aag agc gcg acc gat ttg ggc ggg ctg ccc ggc aag ctg gcc gac 1008
 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335

40
 tgc cgt tcc acc gac ccg cgc aag tcc gaa ctg tat gtg gtg gag ggt 1056
 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350

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 gac tcg gca ggt ggc tcg gcc aag agc ggc cgt gac tcg atg ttc cag 1104
 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365

50
 gcc atc ctg ccg ctg cgc ggc aag atc atc aac gtc gag aag gcc cgc 1152
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380

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 atc gac cgg gtc ctg aag aac acc gaa gtc cag gcg atc atc acc gcg 1200
 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
 385 390 395 400

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 ctg ggt acc ggt att cac gac gag ttc gac att tct aaa ctg cgt tac 1248
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65
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 His Lys Ile Val Leu
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 35 40 45
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
 50 55 60
 15 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu
 65 70 75 80
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
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 20 Thr Ile Asn Leu Thr Asp Glu Arg Val Asp Gln Asp Glu Val Val Asp
 100 105 110
 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Glu Glu Lys
 115 120 125
 25 Ala Ala Glu Ser Lys Ala Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140
 30 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160
 Ser Pro Ile Gln Gln Ser Val Ile Asp Phe Glu Gly Lys Gly Thr Gly
 165 170 175
 35 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
 180 185 190
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
 195 200 205
 40 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
 210 215 220
 Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240
 45 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu
 245 250 255
 Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270
 50 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe

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	275	280	285	
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	290	295	300	
	Ser Ala Gln Ala Arg Ile	Ala Ala Arg Lys Ala	Arg Glu Leu Val Arg	
	305	310	315	320
10	Arg Lys Ser Ala Thr Asp	Leu Gly Gly Leu Pro Gly	Lys Leu Ala Asp	
	325	330	335	
	Cys Arg Ser Thr Asp Pro	Arg Lys Ser Glu Leu Tyr	Val Val Glu Gly	
	340	345	350	
15	Asp Ser Ala Gly Gly Ser	Ala Lys Ser Gly Arg Asp	Ser Met Phe Gln	
	355	360	365	
	Ala Ile Leu Pro Leu Arg	Gly Lys Ile Ile Asn Val	Glu Lys Ala Arg	
	370	375	380	
20	Ile Asp Arg Val Leu Lys	Asn Thr Glu Val Gln	Ala Ile Ile Thr Ala	
	385	390	395	400
	Leu Gly Thr Gly Ile His	Asp Glu Phe Asp Ile	Ser Lys Leu Arg Tyr	
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45	gtg tcg gtg gtc aac gcg ctg tcc acc cgc ctg gag gtc acc atc aag			96
	Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Thr Ile Lys			
	20 25 30			
50	cgc gac ggg cac gag tgg ttt cag tac tac gac cgc gcc gtg ccc gga			144
	Arg Asp Gly His Glu Trp Phe Gln Tyr Tyr Asp Arg Ala Val Pro Gly			
	35 40 45			
55	acc ctc aag cag ggc gag gcc acc aag aag acc gga acc acg atc agg			192
	Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg			
	50 55 60			

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	ttc	tgg	gcg	gag	ccc	gaa	atc	ttc	gaa	acc	aca	cag	tac	gac	ttc	gag	240
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	65					70					75					80	
5	acc	gtg	gcg	cgg	cgg	ctg	cag	gag	atg	gcc	ttc	ctc	aac	aag	ggc	ctc	288
	Thr	Val	Ala	Arg	Arg	Leu	Gln	Glu	Met	Ala	Phe	Leu	Asn	Lys	Gly	Leu	
					85					90					95		
10	acc	atc	aac	ctc	acc	gac	gaa	cga	gtg	gag	cag	gac	gag	gtc	gtc	gac	336
	Thr	Ile	Asn	Leu	Thr	Asp	Glu	Arg	Val	Glu	Gln	Asp	Glu	Val	Val	Asp	
				100					105					110			
15	gag	gtc	gtc	agc	gac	acc	gcc	gag	gca	cgg	aag	tcc	gcc	gaa	gag	aag	384
	Glu	Val	Val	Ser	Asp	Thr	Ala	Glu	Ala	Pro	Lys	Ser	Ala	Glu	Glu	Lys	
			115					120					125				
20	gcc	gcg	gaa	tcg	act	gcg	cca	cac	aag	gtc	aag	cac	cgc	acc	ttc	cac	432
	Ala	Ala	Glu	Ser	Thr	Ala	Pro	His	Lys	Val	Lys	His	Arg	Thr	Phe	His	
			130				135					140					
25	tac	ccc	ggc	ggt	ctg	gtc	gac	ttc	gtc	aag	cac	atc	aac	cgc	acc	aag	480
	Tyr	Pro	Gly	Gly	Leu	Val	Asp	Phe	Val	Lys	His	Ile	Asn	Arg	Thr	Lys	
	145				150						155					160	
30	agc	ccg	atc	cag	cag	agc	gtc	atc	gat	ttc	gac	ggc	aag	ggc	acc	ggc	528
	Ser	Pro	Ile	Gln	Gln	Ser	Val	Ile	Asp	Phe	Asp	Gly	Lys	Gly	Thr	Gly	
					165					170					175		
35	cac	gag	gtc	gag	atc	gcc	atg	cag	tgg	aac	ggc	ggc	tac	tcg	gag	tcc	576
	His	Glu	Val	Glu	Ile	Ala	Met	Gln	Trp	Asn	Gly	Gly	Tyr	Ser	Glu	Ser	
				180					185					190			
40	gtc	cac	acc	ttc	gcc	aac	acc	atc	aac	acg	cac	gag	ggc	ggc	acc	cac	624
	Val	His	Thr	Phe	Ala	Asn	Thr	Ile	Asn	Thr	His	Glu	Gly	Gly	Thr	His	
			195					200					205				
45	gag	gag	ggc	ttc	cgc	agc	gcg	ctg	acg	tcg	gtg	gtg	aac	aag	tac	gcc	672
	Glu	Glu	Gly	Phe	Arg	Ser	Ala	Leu	Thr	Ser	Val	Val	Asn	Lys	Tyr	Ala	
		210					215					220					
50	aaa	gac	aag	aaa	ctg	ctg	aag	gac	aaa	gat	ccc	aac	ctc	acc	ggt	gac	720
	Lys	Asp	Lys	Lys	Leu	Leu	Lys	Asp	Lys	Asp	Pro	Asn	Leu	Thr	Gly	Asp	
		225				230					235					240	
55	gac	atc	cgt	gag	ggc	ttg	gcc	gcg	gtc	atc	tcg	gtg	aag	gtc	gcc	gag	768
	Asp	Ile	Arg	Glu	Gly	Leu	Ala	Ala	Val	Ile	Ser	Val	Lys	Val	Ala	Glu	
					245					250					255		
60	cca	cag	ttc	gaa	ggc	cag	acc	aag	aca	aag	ctg	ggc	aac	acc	gag	gtg	816

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gag gcc aac cca tcc gag gcg aaa acg gtg gtg aac aaa gcg gtg tcg 912
 Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser
 290 295 300
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 tcg gct cag gcg cgc att gcc gcc cgc aag gcg cgt gaa ctg gtg cgc 960
 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320
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 cgc aag agc gcc acc gac ctc ggc ggt ctg ccc ggg aag ctg gcc gac 1008
 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335
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 tgc cgc tcc acc gac ccg cgg aaa tcg gaa ctg tat gtg gtg gag ggc 1056
 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
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 gat tcg gcc ggc ggc tcg gcc aag agc ggg cgc gac tcg atg ttc cag 1104
 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
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 gcg atc ctg ccg ctg cgc ggc aag atc atc aat gtc gag aag gcc cgc 1152
 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
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 atc gac cgg gtg ctg aag aac acc gaa gtt cag gcg atc atc acc gcg 1200
 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
 385 390 395 400
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 ctg ggt acc ggg att cac gac gag ttc gac atc acc aag ctg cgc tat 1248
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 His Lys Ile Val Leu
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 Arg Asp Gly His Glu Trp Phe Gln Tyr Tyr Asp Arg Ala Val Pro Gly
 35 40 45
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 Thr Leu Lys Gln Gly Glu Ala Thr Lys Lys Thr Gly Thr Thr Ile Arg
 50 55 60
 Phe Trp Ala Asp Pro Glu Ile Phe Glu Thr Thr Gln Tyr Asp Phe Glu
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	65		70		75		80
5	Thr Val Ala Arg Arg	85	Leu Gln Glu Met Ala Phe	90	Leu Asn Lys Gly	95	Leu
	Thr Ile Asn Leu Thr Asp Glu Arg Val Glu Gln Asp Glu Val Val Asp	100	105	110			
10	Glu Val Val Ser Asp Thr Ala Glu Ala Pro Lys Ser Ala Glu Glu Lys	115	120	125			
	Ala Ala Glu Ser Thr Ala Pro His Lys Val Lys His Arg Thr Phe His	130	135	140			
15	Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys	145	150	155	160		
	Ser Pro Ile Gln Gln Ser Val Ile Asp Phe Asp Gly Lys Gly Thr Gly	165	170	175			
20	His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser	180	185	190			
	Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His	195	200	205			
25	Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala	210	215	220			
	Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp	225	230	235	240		
30	Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ala Glu	245	250	255			
	Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val	260	265	270			
35	Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe	275	280	285			
	Glu Ala Asn Pro Ser Glu Ala Lys Thr Val Val Asn Lys Ala Val Ser	290	295	300			
40	Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg	305	310	315	320		
	Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp	325	330	335			
45	Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly	340	345	350			
50	Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln	355	360	365			
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Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
370 375 380

5 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr
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10 His Lys Ile Val Leu
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<210> 35
20 <211> 1260
15 <212> DNA
<213> Mycobacterium branderi

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20 <222> (1)..(1260)

<400> 35

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25 gtg tcg gtg gtc aac gca ttg tcg act cga ctc gag gtg gag atc gcc 96
Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Glu Ile Ala
20 25 30

30 acc gac ggg tac gag tgg ttt cag cat tac gac cgc tct gtc ccc gcc 144
Thr Asp Gly Tyr Glu Trp Phe Gln His Tyr Asp Arg Ser Val Pro Gly
35 40 45

35 acg ctc aag caa ggc gag aaa acc aaa aag acc ggc acc acg gtc cgc 192
Thr Leu Lys Gln Gly Glu Lys Thr Lys Lys Thr Gly Thr Thr Val Arg
50 55 60

40 ttc tgg gcc gac ccg gac atc ttc gag acg acg gat tac gac ttc gag 240
Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Asp Tyr Asp Phe Glu
65 70 75 80

45 acg gtc gca cgc cgg ctg cag gaa atg gcg ttc ctc aac aaa ggg ctg 288
Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
85 90 95

50 acc atc aac ctg acc gac gag cgg gtg cga aac gaa gaa gtc gtc gac 336
Thr Ile Asn Leu Thr Asp Glu Arg Val Arg Asn Glu Glu Val Val Asp
100 105 110

55 gag gtc gtc agc gac acc gcc gac gcg ccg aag tcg gcg cgc gaa gag 384
Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Arg Glu Glu
115 120 125

gcc gaa gaa cgg acc acg cag aaa gtc aag cac cgc acg ttc cat tac 432

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	Ala	Glu	Glu	Arg	Thr	Thr	Gln	Lys	Val	Lys	His	Arg	Thr	Phe	His	Tyr	
	130						135					140					
5	ccc	ggc	ggc	ttg	gtc	gat	ttc	gtc	aaa	cac	atc	aac	cgc	aca	aag	aac	480
	Pro	Gly	Gly	Leu	Val	Asp	Phe	Val	Lys	His	Ile	Asn	Arg	Thr	Lys	Asn	160
	145					150					155						
10	ccc	atc	cat	tcg	agc	atc	gtc	gac	ttc	tcc	ggc	aag	ggt	ccc	ggc	cac	528
	Pro	Ile	His	Ser	Ser	Ile	Val	Asp	Phe	Ser	Gly	Lys	Gly	Pro	Gly	His	175
					165					170							
15	gag	gtc	gag	atc	gca	atg	cag	tgg	aac	gcc	ggc	tat	tcg	gag	tcg	gtg	576
	Glu	Val	Glu	Ile	Ala	Met	Gln	Trp	Asn	Ala	Gly	Tyr	Ser	Glu	Ser	Val	190
					180				185								
20	cac	acc	ttc	gcc	aac	acc	atc	aac	acc	cac	gag	ggc	ggc	acc	cac	gaa	624
	His	Thr	Phe	Ala	Asn	Thr	Ile	Asn	Thr	His	Glu	Gly	Gly	Thr	His	Glu	205
			195					200									
25	gaa	ggg	ttc	cgc	gcg	gca	ctg	acg	tcc	gtg	gtg	aac	aag	tac	gcc	aag	672
	Glu	Gly	Phe	Arg	Ala	Ala	Leu	Thr	Ser	Val	Val	Asn	Lys	Tyr	Ala	Lys	220
		210					215										
30	gac	cga	aaa	ctg	ctg	aag	gac	aag	gac	ccc	aac	ctc	acc	ggc	gac	gac	720
	Asp	Arg	Lys	Leu	Leu	Lys	Asp	Lys	Asp	Pro	Asn	Leu	Thr	Gly	Asp	Asp	235
	225					230					235					240	
35	att	cgt	gag	ggc	ctg	gcg	gcg	gtc	atc	tcg	gtc	aag	gtc	agc	gag	ccg	768
	Ile	Arg	Glu	Gly	Leu	Ala	Ala	Val	Ile	Ser	Val	Lys	Val	Ser	Glu	Pro	250
					245					250					255		
40	cag	ttc	gag	ggc	cag	acc	aaa	acc	aaa	ctc	ggc	aac	acc	gaa	gtc	aag	816
	Gln	Phe	Glu	Gly	Gln	Thr	Lys	Thr	Lys	Leu	Gly	Asn	Thr	Glu	Val	Lys	265
				260					265					270			
45	tcg	ttt	gtg	cag	aag	gtc	tgc	aac	gaa	cag	ctc	acc	cac	tgg	ttc	gag	864
	Ser	Phe	Val	Gln	Lys	Val	Cys	Asn	Glu	Gln	Leu	Thr	His	Trp	Phe	Glu	280
			275					280					285				
50	gcc	aat	ccc	agc	gac	gcc	aag	acc	gtc	gtc	aac	aaa	gcg	gtg	tcg	tcg	912
	Ala	Asn	Pro	Ser	Asp	Ala	Lys	Thr	Val	Val	Asn	Lys	Ala	Val	Ser	Ser	295
		290					295				300						
55	gcg	cag	gcc	cgc	att	gcc	gcc	cgc	aaa	gcg	cga	gaa	ttg	gtg	cgc	cgc	960
	Ala	Gln	Ala	Arg	Ile	Ala	Ala	Arg	Lys	Ala	Arg	Glu	Leu	Val	Arg	Arg	310
						310					315					320	
60	aag	agc	gca	acc	gat	ctt	ggc	ggg	ctg	ccg	ggc	aag	ctg	gct	gac	tgc	1008
	Lys	Ser	Ala	Thr	Asp	Leu	Gly	Gly	Leu	Pro	Gly	Lys	Leu	Ala	Asp	Cys	325
					325					330					335		
65	cgc	tcg	acc	gat	cca	cgc	aag	tcc	gaa	ttg	tat	gtg	gtg	gag	ggt	gat	1056
	Arg	Ser	Thr	Asp	Pro	Arg	Lys	Ser	Glu	Leu	Tyr	Val	Val	Glu	Gly	Asp	340
					340				345					350			
70	tcg	gcc	ggc	ggc	tcg	gcc	aag	agc	ggc	cgc	gac	tcg	atg	ttt	cag	gcg	1104

Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala
 355 360 365
 5 atc ctg ccg ttg cgg ggc aag atc atc aac gtg gag aag gcc cgc atc 1152
 Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile
 370 375 380
 10 gac cgg gtg ctg aag aac act gag gtg cag gcg atc atc acc gcg ctg 1200
 Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu
 385 390 395 400
 15 ggc acc ggg att cac gac gag ttc gac atc tcc aag ctg cgc tac cac 1248
 Gly Thr Gly Ile His Asp Glu Phe Asp Ile Ser Lys Leu Arg Tyr His
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 aag atc gtg ctg 1260
 Lys Ile Val Leu
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 Thr Asp Gly Tyr Glu Trp Phe Gln His Tyr Asp Arg Ser Val Pro Gly
 35 35 40 45
 35 Thr Leu Lys Gln Gly Glu Lys Thr Lys Lys Thr Gly Thr Thr Val Arg
 50 55 60
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Asp Tyr Asp Phe Glu
 65 70 75 80
 40 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
 85 90 95
 Thr Ile Asn Leu Thr Asp Glu Arg Val Arg Asn Glu Glu Val Val Asp
 100 105 110
 45 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Arg Glu Glu
 115 120 125
 Ala Glu Glu Arg Thr Thr Gln Lys Val Lys His Arg Thr Phe His Tyr
 130 135 140
 50 Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn
 145 150 155 160
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Pro Ile His Ser Ser Ile Val Asp Phe Ser Gly Lys Gly Pro Gly His
165 170 175

5 Glu Val Glu Ile Ala Met Gln Trp Asn Ala Gly Tyr Ser Glu Ser Val
180 185 190

His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu
195 200 205

10 Glu Gly Phe Arg Ala Ala Leu Thr Ser Val Val Asn Lys Tyr Ala Lys
210 215 220

Asp Arg Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp Asp
225 230 235 240

15 Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro
245 250 255

Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val Lys
260 265 270

20 Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe Glu
275 280 285

Ala Asn Pro Ser Asp Ala Lys Thr Val Val Asn Lys Ala Val Ser Ser
290 295 300

25 Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg
305 310 315 320

Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys
325 330 335

30 Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp
340 345 350

35 Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala
355 360 365

Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile
370 375 380

40 Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala Leu
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Gly Thr Gly Ile His Asp Glu Phe Asp Ile Ser Lys Leu Arg Tyr His
405 410 415

45 Lys Ile Val Leu
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<213> Mycobacterium paratuberculosis

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 <222> (1)..(1263)

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gtc tcg gtg gtc aac gcg ctg tcc act cgg ctc gag gtc aac atc gcc 96
 Val Ser Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Asn Ile Ala
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cgc gac ggc tac gag tgg tcg cag tac tac gac cac gcc gtg ccc ggc 144
 Arg Asp Gly Tyr Glu Trp Ser Gln Tyr Tyr Asp His Ala Val Pro Gly
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acc ctc aag cag ggc gag gcc acc aag cgc acc ggc acc acc atc cgg 192
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg
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ttc tgg gcc gac ccc gac atc ttc gag acc acc gag tac gac ttc gaa 240
 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
 65 70 75 80

25

acg gtg gcc cgg cgg ctg cag gaa atg gcg ttc ctc aac aag ggc ctg 288
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
 85 90 95

30

acc atc aac ctc acc gac gag cgg gtg acc aac gaa gag gtc gtc gac 336
 Thr Ile Asn Leu Thr Asp Glu Arg Val Thr Asn Glu Glu Val Val Asp
 100 105 110

35

gag gtg gtc agc gac acc gcc gac gca ccc aag tcg gcg cag gag aag 384
 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys
 115 120 125

gcg gcg gaa tcg gct gcg ccg cat aag gtc aag cac cgc acc ttc cac 432
 Ala Ala Glu Ser Ala Ala Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140

40

tac ccc ggc ggc ctg gtc gac ttc gtc aaa cac atc aat cgc acc aaa 480
 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160

45

aac ccc atc cac cag agc atc atc gat ttc ggt ggg aag ggc ccc ggc 528
 Asn Pro Ile His Gln Ser Ile Ile Asp Phe Gly Gly Lys Gly Pro Gly
 165 170 175

cac gag gtc gag atc gcg atg cag tgg aac ggc ggc tac tcc gaa tcg 576
 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
 180 185 190

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gtg cac acc ttc gcc aac acc atc aac acg cac gag ggc ggc acc cac 624
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His

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	195	200	205	
5	gag gag ggc ttc cgc agc gcg ctg acc tcc gtg gtc aac aag tac gcc Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala 210 215 220			672
10	aag gac aag aag ctg ctc aag gac aag gac ccc aac ctg acc ggt gac Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp 225 230 235 240			720
15	gac atc cgc gag ggt ttg gcc gcg gtg atc tcg gtc aag gtg agc gaa Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu 245 250 255			768
20	ccg cag ttc gag ggc cag acc aag acc aaa ctg ggc aac acc gag gtg Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val 260 265 270			816
25	aag tcg ttc gtg cag aag gtg tgc aac gaa cag ctc acc cac tgg ttc Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe 275 280 285			864
30	gaa gcc aac ccc gca gac gcc aaa gtc att gtc aac aag gcg gtt tca Glu Ala Asn Pro Ala Asp Ala Lys Val Ile Val Asn Lys Ala Val Ser 290 295 300			912
35	tca gcg cag gcg cgc atc gcc gcg cgc aag gcg cga gag ttg gtg cgc Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg 305 310 315 320			960
40	cgc aag agc gca acc gac ctg ggc ggg ctg ccc ggc aag ctc gcc gac Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp 325 330 335			1008
45	tgc cgg tcg acc gac ccg cgc aag tcg gaa ttg tat gtg gtc gag ggt Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly 340 345 350			1056
50	gac tcg gcc ggc ggc tcg gcg aaa agc ggc cgg gac tcg atg ttc cag Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln 355 360 365			1104
55	gcc atc ctt ccg ctg cgc ggc aag atc atc aac gtc gaa aag gcc cgc Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg 370 375 380			1152
60	atc gac cgg gtg ctg aag aac acc gag gtg cag gcg atc atc acc gcg Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala 385 390 395 400			1200
65	ctg ggc acc ggg att cac gac gag ttc gac atc acc aag ctg cgc tac Leu Gly Thr Gly Ile His Asp Glu Phe Asp Ile Thr Lys Leu Arg Tyr 405 410 415			1248
70	cac aag atc gtg ttg His Lys Ile Val Leu			1263

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 35 40 45
 Thr Leu Lys Gln Gly Glu Ala Thr Lys Arg Thr Gly Thr Thr Ile Arg
 50 55 60
 20 Phe Trp Ala Asp Pro Asp Ile Phe Glu Thr Thr Glu Tyr Asp Phe Glu
 65 70 75 80
 Thr Val Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu
 85 90 95
 25 Thr Ile Asn Leu Thr Asp Glu Arg Val Thr Asn Glu Glu Val Val Asp
 100 105 110
 Glu Val Val Ser Asp Thr Ala Asp Ala Pro Lys Ser Ala Gln Glu Lys
 115 120 125
 30 Ala Ala Glu Ser Ala Ala Pro His Lys Val Lys His Arg Thr Phe His
 130 135 140
 35 Tyr Pro Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys
 145 150 155 160
 Asn Pro Ile His Gln Ser Ile Ile Asp Phe Gly Gly Lys Gly Pro Gly
 165 170 175
 40 His Glu Val Glu Ile Ala Met Gln Trp Asn Gly Gly Tyr Ser Glu Ser
 180 185 190
 Val His Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His
 195 200 205
 45 Glu Glu Gly Phe Arg Ser Ala Leu Thr Ser Val Val Asn Lys Tyr Ala
 210 215 220
 Lys Asp Lys Lys Leu Leu Lys Asp Lys Asp Pro Asn Leu Thr Gly Asp
 225 230 235 240
 50 Asp Ile Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu
 245 250 255

55

Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Thr Glu Val
 260 265 270
 5 Lys Ser Phe Val Gln Lys Val Cys Asn Glu Gln Leu Thr His Trp Phe
 275 280 285
 Glu Ala Asn Pro Ala Asp Ala Lys Val Ile Val Asn Lys Ala Val Ser
 290 295 300
 10 Ser Ala Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg
 305 310 315 320
 Arg Lys Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp
 325 330 335
 15 Cys Arg Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly
 340 345 350
 Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln
 355 360 365
 20 Ala Ile Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg
 370 375 380
 Ile Asp Arg Val Leu Lys Asn Thr Glu Val Gln Ala Ile Ile Thr Ala
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 Val Val Asn Ala Leu Ser Thr Arg Leu Glu Val Glu Ile Lys Arg Asp
 20 25 30
 50 ggc cat gag tgg tcg cag gtt tac gag aaa tcc gag ccg atg gga ctc 144
 Gly His Glu Trp Ser Gln Val Tyr Glu Lys Ser Glu Pro Met Gly Leu
 35 40 45
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5 aag caa ggc gcg cag act aag aag acc ggc acg acg gtc cgg ttc tgg 192
Lys Gln Gly Ala Pro Thr Lys Lys Thr Gly Thr Thr Val Arg Phe Trp
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10 gcc gat ccc aat gtt ttt gag acc acc gag tac gac ttc gaa acc gtc 240
Ala Asp Pro Asn Val Phe Glu Thr Thr Gly Tyr Asp Phe Glu Thr Val
65 70 75 80

15 gca cga cgg ttg cag gag atg gcg ttt ctc aac aag ggg ctc acc atc 288
Ala Arg Arg Leu Gln Glu Met Ala Phe Leu Asn Lys Gly Leu Thr Ile
85 90 95

20 aat ctg acc gat cag cgg gtg acc cag gac gag gtc gtc gac gag gtg 336
Asn Leu Thr Asp Gln Arg Val Thr Gln Asp Glu Val Val Asp Glu Val
100 105 110

25 gtc agc gac gtc gcc gag gcc cca aag tgc gcc agc gag aag gcg gcc 384
Val Ser Asp Val Ala Glu Ala Pro Lys Ser Ala Ser Glu Lys Ala Ala
115 120 125

30 gaa tcc gcc gcc cag cac aag gtc aag aag cgt acc ttc cac tat ccc 432
Glu Ser Ala Ala Pro His Lys Val Lys Lys Arg Thr Phe His Tyr Pro
130 135 140

35 ggg ggt ctg gtt gac ttc gtc aag cac atc aac cgg acc aag aac gcc 480
Gly Gly Leu Val Asp Phe Val Lys His Ile Asn Arg Thr Lys Asn Ala
145 150 155 160

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45 gtc gag atc gcg atg cag tgg aat gcc ggc tat tgc gag tgc gtc cat 576
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50 acc ttc gcc aac acc atc aac acc cac gag ggt ggg acc cac gaa gag 624
Thr Phe Ala Asn Thr Ile Asn Thr His Glu Gly Gly Thr His Glu Glu
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55 ggg ttc cgc agc gcg ctg acc tgc gtg gtg aac aag tac gcc aag gac 672
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65 cgg gaa ggg ttg gcc gcg gtg att tgc gtc aag gtc agc gag ccg cag 768
Arg Glu Gly Leu Ala Ala Val Ile Ser Val Lys Val Ser Glu Pro Gln
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70 ttc gag ggc cag acc aag acg aaa ctg ggc aac acc gag gtg aag tgc 816
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EP 1 098 003 A2

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 5 Ala Asp Pro Asn Val Phe Glu Thr Thr Glu Tyr Asp Phe Glu Thr Val
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 115 120 125
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 40 Asn Pro Ala Asp Ala Lys Thr Val Val Asn Lys Ala Val Ser Ser Ala
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 Gln Ala Arg Ile Ala Ala Arg Lys Ala Arg Glu Leu Val Arg Arg Lys
 305 310 315 320
 Ser Ala Thr Asp Leu Gly Gly Leu Pro Gly Lys Leu Ala Asp Cys Arg
 325 330 335
 50 Ser Thr Asp Pro Arg Lys Ser Glu Leu Tyr Val Val Glu Gly Asp Ser
 340 345 350

55

Ala Gly Gly Ser Ala Lys Ser Gly Arg Asp Ser Met Phe Gln Ala Ile
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 5 Leu Pro Leu Arg Gly Lys Ile Ile Asn Val Glu Lys Ala Arg Ile Asp
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17

Claims

1. A method for identifying a slow growing mycobacteria species, which comprises amplifying the regions corresponding to SEQUENCE NO. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39 in the DNA which encodes DNA gyrase β subunit of a slow growing mycobacteria in a sample, determining and comparing the nucleotide sequence of the amplified fragment with the nucleotide sequences described in SEQUENCE NO. 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37 and 39, thereby calculating a genetic distance of the sequence of the amplified fragment from each sequence, and identifying the species of the slow growing mycobacteria in a sample based on the genetic distance.
2. A method for detecting *Mycobacterium kansasii*, which comprises detecting *Mycobacterium kansasii* using, as a primer or probe, an oligonucleotide which comprises a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 4, or a complementary sequence thereof, and substantially functions as a primer or probe.
3. A *Mycobacterium kansasii* detection kit which comprises an oligonucleotide which comprises a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 4, or a complementary sequence thereof, and substantially functions as a primer or probe.
4. A method for detecting *Mycobacterium gastri*, which comprises detecting *Mycobacterium gastri* using, as a primer or probe, an oligonucleotide which comprises a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 6, or a complementary sequence thereof, and substantially functions as a primer or probe.
5. A *Mycobacterium gastri* detection kit which comprises an oligonucleotide which comprises a sequence coding for a part of or the entire portion of the amino acid sequence described in SEQUENCE NO. 6, or its complementary sequence, and substantially functions as a primer or probe.
6. A method for identifying a slow growing mycobacteria species, which comprises
checking, in DNA of a sample, the existence of a DNA comprising a unique region having a different nucleotide sequence in the DNA sequence coding for DNA gyrase β subunit among slow growing mycobacteria,
identifying a bacterium in a sample based on the existence of said DNA as a marker.
7. The method for identifying a slow growing mycobacteria species according to claim 6, wherein the slow growing mycobacteria are *Mycobacterium simiae*, *Mycobacterium bovis*, *Mycobacterium szulgai*, *Mycobacterium malmoense*, *Mycobacterium intracellulare*, *Mycobacterium avium*, *Mycobacterium gordonae*, *Mycobacterium africanum*.

num, Mycobacterium tuberculosis, Mycobacterium gastr, Mycobacterium marinum, Mycobacterium microti, Mycobacterium asiaticum, Mycobacterium scrofulaceum, Mycobacterium branderi, Mycobacterium paratuberculosis, and Mycobacterium kansasii.

- 5 8. The method for identifying a slow growing mycobacteria species according to claim 6, which comprises the following steps (1) to (4):

(1) synthesizing an oligonucleotide which comprises a unique region having a different nucleotide sequence in the DNA sequence coding for DNA gyrase β subunit among slow growing mycobacteria,
10 (2) preparing a solution which comprises the oligonucleotide synthesized in the step (1), dNTP, DNA polymerase and a bacterial DNA in a sample,
(3) heating the solution prepared in the step (2) repeatedly under such conditions that polymerase chain reaction can occur, and
15 (4) subjecting the solution obtained in the step (3) to electrophoresis to identify the species of the bacterium in a sample based on the electrophoresis pattern.

9. The method for identifying a slow growing mycobacteria species according to claim 8, wherein the oligonucleotide is an oligonucleotide which encodes the amino acid sequence described in SEQUENCE NO. 46, SEQUENCE NO. 48, SEQUENCE NO. 50, SEQUENCE NO. 52, SEQUENCE NO. 54, SEQUENCE NO. 56 or SEQUENCE NO. 58.

- 20 10. The method for identifying a slow growing mycobacteria species according to claim 8, wherein the oligonucleotide is an oligonucleotide represented by SEQUENCE NO. 45, SEQUENCE NO. 47, SEQUENCE NO. 49, SEQUENCE NO. 51, SEQUENCE NO. 53, SEQUENCE NO. 55 or SEQUENCE NO. 57.

- 25 11. The method for identifying a slow growing mycobacteria species according to claim 6, which comprises the following steps (1) to (4):

(1) synthesizing a first oligonucleotide which is identical to a first partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria and a second oligonucleotide which is complementary to a second partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria, said first partial sequence and said second partial sequence being respectively conserved among slow growing mycobacteria,
30 (2) subjecting the two oligonucleotides synthesized in the step (1) as primers and a bacterial DNA sample as a template to the polymerase chain reaction,
35 (3) mixing the DNA fragment amplified in the step (2) with a restriction enzyme under the conditions at which the restriction enzyme is active, said restriction enzyme recognizing the sequence unique to one or more slow growing mycobacteria, and
(4) subjecting the mixture obtained in the step (3) to electrophoresis to identify the species of the bacterium in a sample based on the electrophoresis pattern.

- 40 12. The method for identifying a slow growing mycobacteria species according to claim 11, wherein the two oligonucleotides to be used as primers are oligonucleotides represented by SEQUENCE NO. 1 and SEQUENCE NO. 3, and the restriction enzymes to be used are *Rsa* I and *Taq* I.

- 45 13. An identification kit for a slow growing mycobacteria species, which comprises an oligonucleotide containing a region of DNA coding for DNA gyrase β subunit, a region having different nucleotide sequence among slow growing mycobacteria.

- 50 14. An identification kit for a slow growing mycobacteria species, which comprises

a first oligonucleotide which is identical to a first partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria,
a second oligonucleotide which is complementary to a second partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria, said first partial sequence and said second partial
55 sequence being respectively conserved among slow growing mycobacteria, and
one or more restriction enzyme recognizing the sequence unique to one or more slow growing mycobacteria.

15. A method for detecting a slow growing mycobacteria species, which comprises

checking, in DNA of a sample, the existence of a DNA comprising a unique region having a different nucleotide sequence in the DNA sequence coding for DNA gyrase β subunit among slow growing mycobacteria, detecting a bacterium in a sample based on the existence of said DNA as a marker.

- 5 16. The method for detecting a slow growing mycobacteria species according to claim 15, wherein the slow growing mycobacteria are *Mycobacterium simiae*, *Mycobacterium bovis*, *Mycobacterium szulgai*, *Mycobacterium malmoense*, *Mycobacterium intracellulare*, *Mycobacterium avium*, *Mycobacterium gordonae*, *Mycobacterium africanum*, *Mycobacterium tuberculosis*, *Mycobacterium gastr*, *Mycobacterium marinum*, *Mycobacterium microti*, *Mycobacterium asiaticum*, *Mycobacterium scrofulaceum*, *Mycobacterium branderi*, *Mycobacterium paratuberculosis*, and *Mycobacterium kansasii*.

17. The method for detecting a slow growing mycobacteria species according to claim 15, which comprises the following steps (1) to (4):

- 15 (1) synthesizing an oligonucleotide which comprises a unique region having a different nucleotide sequence in the DNA sequence coding for DNA gyrase β subunit among slow growing mycobacteria,
(2) preparing a solution which comprises the oligonucleotide synthesized in the step (1), dNTP, DNA polymerase and a bacterial DNA in a sample,
20 (3) heating the solution prepared in the step (2) repeatedly under such conditions that polymerase chain reaction can occur, and
(4) subjecting the solution obtained in the step (3) to electrophoresis to detecting the bacterium in a sample based on the electrophoresis pattern.

- 25 18. The method for detecting a slow growing mycobacteria species according to claim 17, wherein the oligonucleotide is an oligonucleotide which encodes the amino acid sequence described in SEQUENCE NO. 46, SEQUENCE NO. 48, SEQUENCE NO. 50, SEQUENCE NO. 52, SEQUENCE NO. 54, SEQUENCE NO. 56 or SEQUENCE NO. 58.

- 30 19. The method for detecting a slow growing mycobacteria species according to claim 17, wherein the oligonucleotide is an oligonucleotide represented by SEQUENCE NO. 45, SEQUENCE NO. 47, SEQUENCE NO. 49, SEQUENCE NO. 51, SEQUENCE NO. 53, SEQUENCE NO. 55 or SEQUENCE NO. 57.

20. The method for detecting a slow growing mycobacteria species according to claim 15, which comprises the following steps (1) to (4):

- 35 (1) synthesizing a first oligonucleotide which is identical to a first partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria and a second oligonucleotide which is complementary to a second partial sequence in the DNA sequence coding for the DNA gyrase β subunit of slow growing mycobacteria, said first partial sequence and said second partial sequence being respectively conserved among slow growing mycobacteria,
40 (2) subjecting the two oligonucleotides synthesized in the step (1) as primers and a bacterial DNA sample as a template to the polymerase chain reaction,
(3) mixing the DNA fragment amplified in the step (2) with a restriction enzyme under the conditions at which the restriction enzyme is active, said restriction enzyme recognizing the sequence unique to one or more slow growing mycobacteria, and
45 (4) subjecting the mixture obtained in the step (3) to electrophoresis to detect the bacterium in a sample based on the electrophoresis pattern.

- 50 21. The method for detecting a slow growing mycobacteria species according to claim 20, wherein the two oligonucleotides to be used as primers are oligonucleotides represented by SEQUENCE NO. 1 and SEQUENCE NO. 3, and the restriction enzymes to be used are *Rsa* I and *Taq* I.

22. A detection kit for a slow growing mycobacteria species, which comprises an oligonucleotide containing a region of DNA coding for DNA gyrase β subunit, a region having different nucleotide sequence among slow growing mycobacteria.

- 55 23. A detection kit for a slow growing mycobacteria species, which comprises

a first oligonucleotide which is identical to a first partial sequence in the DNA sequence coding for the DNA

gyrase β subunit of slow growing mycobacteria,
a second oligonucleotide which is complementary to a second partial sequence in the DNA sequence coding
for the DNA gyrase β subunit of slow growing mycobacteria, said first partial sequence and said second partial
sequence being respectively conserved among slow growing mycobacteria, and
5 one or more restriction enzyme recognizing the sequence unique to one or more slow growing mycobacteria.

24. A method for identifying a slow growing mycobacteria species, which comprises the following steps (1) to (4):

- 10 (1) synthesizing an oligonucleotide which comprises a sequence corresponding to a region in the DNA gyrase β subunit wherein the 3'-side nearest neighbor base to said region in the DNA gyrase β subunit is a unique base among the slow growing mycobacteria,
- (2) preparing a solution which comprises the oligonucleotide synthesized in the step (1), a labeled ddNTP, DNA polymerase, and a bacterial DNA in a sample,
- 15 (3) heating the solution prepared in the step (2) under such conditions that reaction between the labeled ddNTP and the oligonucleotide occurs,
- (4) checking the existence of the labeled oligonucleotide, and
- (5) identifying a bacterium in a sample based on the existence of the labeled oligonucleotide.

25. A method for detecting a slow growing mycobacteria species, which comprises the following steps (1) to (4):

- 20 (1) synthesizing an oligonucleotide which comprises a sequence corresponding to a region in the DNA gyrase β subunit wherein the 3'-side nearest neighbor base to said region in the DNA gyrase β subunit is a unique base among the slow growing mycobacteria,
- (2) preparing a solution which comprises the oligonucleotide synthesized in the step (1), a labeled ddNTP, DNA polymerase, and a bacterial DNA in a sample,
- 25 (3) heating the solution prepared in the step (2) under such conditions that reaction between the labeled ddNTP and the oligonucleotide occurs,
- (4) checking the existence of the labeled oligonucleotide, and
- 30 (5) detecting a bacterium in a sample based on the existence of the labeled oligonucleotide.

Fig. 1

KPM2201	GGCGAGAACAGCGGCTACACGGTCAGCGGTGGGTTGCACGGCGTGGGCGTGTGGTGGTT
ATCC25274	GGTGAGAACAGCGGCTACACGGTCAGCGGTGGGCTGCACGGTGTGGTGTGTCAAGTGGTC
KPM1403	GGGGAGAACAGTGGCTACACGGTCAGCGGCGGGTTGCACGGGTCGGAGTGTGGTGGTC
KPM2027	GGCGAGAACAGCGGCTACACGGTCAGCGGTGGGTTGCACGGAGTGGGCGTGTGGTGGTC
KPM1201	GGCGAGAACAGTGGTTACAACGTCAAGTGGTGGTCTGCACGGCGTGGTGTGTGGTGGTC
KPM2403	GGCGAGAACAGTGGCTACAACGTCAAGTGGTGGTCTGCACGGCGTGGGCGTGTGGTGGTC
KPM3012	GGCGAGAACAGCGGCTACAACGTCAAGCGGCGTCTGCACGGCGTGGGCGTGTGGTGGTC
Bovine10	GGCGAGAACAGCGGCTACAACGTCAAGCGGCGTCTGCACGGCGTGGGCGTGTGGTGGTC
KPM3101	GGTGAGAACAGCGGTACAACGTCAAGCGGTGGCTGCACGGCGTGGGCGTGTGGTGGTC
KPM3401	GGCGAGAACAGCGGATACAACGTCAAGTGGCGGTTTGCACGGTGTGGGCGTGTGGTGGTC
ATCC51789	GGCGATGACAGCGCCTACGCGGTCTGGGTTGGTCTGCACGGCGTGGGCGTGTGGTGGTC
T801	-----TCGGACGCGTATGCGATATCTGGTGGTCTGCACGGCGTGGGCGTGTGGTGGTT
T901	-----TCGGACGCGTATGCGATATCTGGTGGTCTGCACGGCGTGGGCGTGTGGTGGTT
T704	-----TCGGACGCGTATGCGATATCTGGTGGTCTGCACGGCGTGGGCGTGTGGTGGTT
T021	-----TCGGACGCGTATGCGATATCTGGTGGTCTGCACGGCGTGGGCGTGTGGTGGTT
KPM3504	-----TCCGACGCGTATGCGATATCGGGTGGAGTGCACGGTGTGGGTTGTCTGGTGGTC
KPM1001	-----TCCGACGCGTACGCGATATCGGGCGGGCTGCACGGTGTGGGTTGTCTGGTGGTC 60
Sequence No. 41	----- * * * * *
Sequence No. 61	----- * * * * *
Sequence No. 62	----- * * * * *
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ATCC25274	AACGCGTTGTGACCCGACTCGAGGTGACATCAAGCGCGACGGGCACGAGTGGTCCAG
KPM1403	AACGCGCTGTCCACCCGCTGGAAGTCAACGTCAAGCGTGACGGCTATGAGTGGTCCAG
KPM2027	AACGCGCTGTCCACCCGCTGGAAGTCAACGTCAAGCGTGACGGCTATGAGTGGTCCAG
KPM1201	AACGCGCTGTCCACCCGACTGGAAGTCGACATCAAGCGCGACGATACGAGTGGTCCAG
KPM2403	AACGCGCTGTGACCCGGCTCGAGGTGACATCAAGCGTGACGGCCACAAGTGGTCCAG
KPM3012	AACGCGCTGTCCACTCGGCTCGAGGTCAACATCGCCCGGACGGCTACGAGTGGTCCAG
Bovine10	AACGCGCTGTCCACTCGGCTCGAGGTCAACATCGCCCGGACGGCTACGAGTGGTCCAG
KPM3101	AACGCGCTGTGACCCGGCTCGAGGTGGAGATCGCCCGGATGGCTACGAATGGTCCAG
KPM3401	AACGCGTTGTGACCCGGCTCGAGGTGGATGTGCGCCGGACGGCTACATGTGGTCCAG
ATCC51789	AACGCATTGTGACTCGACTCGAGGTGGAGATCGCGACCGAGGGTACGAGTGGTTCCAG
T801	AACGCGCTATCCACCCGGCTCGAAGTCGAGATCAAGCGCGACGGGTACGAGTGGTCTCAG
T901	AACGCGCTATCCACCCGGCTCGAAGTCGAGATCAAGCGCGACGGGTACGAGTGGTCTCAG
T704	AACGCGCTATCCACCCGGCTCGAAGTCGAGATCAAGCGCGACGGGTACGAGTGGTCTCAG
T021	AACGCGCTATCCACCCGGCTCGAAGTCGAGATCAAGCGCGACGGGTACGAGTGGTCTCAG
KPM3504	AACGCGCTGTCCATCCGGTGGAGGTGGAGATCAAGCGCGACGGCCATGAGTGGTCCAA
KPM1001	AACGCACTGTCCACCCGGTGGAGGTGGAGATCAAGCGCGACGGCCATGAGTGGTCCAG 120
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Sequence No. 55	*****

Fig. 2

KPM2201	TATTACAAGCGCGGGTGCCGGGCACCCCTCAAGCAGGGTGAGACGACCCGCAAGACCGGC
ATCC25274	TATTACGAGCGCGCCGTTCTGGCAGGCTCAAGCAGGGCGAGGCGACCAAGAAGACCGGC
KPM1403	TACTACGACCGGGCGGTTGCCGGGCACCCCTCAAGCAAGGCGAGGCGACCAAGAAGACCGGC
KPM2027	TACTACGACCGCGCCGTTGCCGGGAACCCCTCAAGCAGGGCGAGGCGACCAAGAAGACCGGA
KPM1201	TTCTACGACCGCGCCGAGCCGGGCACCCCTCAAACAGGGCGAGGCAACCAAGAAGACCGGA
KPM2403	TTCTACAACAAGGCCGTGCCGGGCACGCTCAAACAGGGTGAGGCCACTAAGAAAACCGGA
KPM3012	TACTACGACCGCGCCGTTGCCGGGCACCCCTCAAGCAGGGCGAGGCGACCAAGCGCAGCGGC
Bovine10	TACTACGACCGCGCCGTTGCCGGGCACCCCTCAAGCAGGGCGAGGCGACCAAGCGCAGCGGC
KPM3101	TTCTACGACCGCGGTAACCGGAACGCTCAAACAGGGTGAGGCCACCAAGCGGACCGGC
KPM3401	TTCTACGATCAGCGCGAGCCGGGAACCCCTCAAACAGGGCGAGGCGACCAAGACGACGGGA
ATCC51789	CATTACGACCGCTCTGTCCCGGCGAGCTCAAGCAAGGGCGAGAAAACCAAAAAGACCGGC
T801	GTTTATGAGAAGTCGGAACCCCTGGGCCTCAAGCAAGGGGCGCGGACCAAGAAGACGGGG
T901	GTTTATGAGAAGTCGGAACCCCTGGGCCTCAAGCAAGGGGCGCGGACCAAGAAGACGGGG
T704	GTTTATGAGAAGTCGGAACCCCTGGGCCTCAAGCAAGGGGCGCGGACCAAGAAGACGGGG
T021	GTTTATGAGAAGTCGGAACCCCTGGGCCTCAAGCAAGGGGCGCGGACCAAGAAGACGGGG
KPM3504	GTTTATGAGAAGTCGGAACCCCTGGGCCTCAAGCAAGGGGCGCGGACCAAGAAGACCGGC
KPM1001	GTTTACGAGAAATCCGAGCCGATGGGACTCAAGCAAGGGGCGCGGACTAAGAAGACCGGC 180

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Sequences No. 45, 49

KPM2201	ACCACAATCCGGTTCTGGGCGGATCCGGAGATCTTCGAGACCACCAATACGACTTCGAG
ATCC25274	ACCACCATCCGGTTCTGGGCGGACCCGGACATCTTCGAGACCACCAAGTACGACTTCGAG
KPM1403	ACCACGATCCGGTTCTGGGCGGATCCTGAGATCTTCGAAACCACCAAGTACGACTTCGAG
KPM2027	ACCACGATCAGGTTCTGGGCGGACCCGAAATCTTCGAAACCACACAGTACGACTTCGAG
KPM1201	ACCACCATCCGGTTCTGGGCGGACTCGGACATCTTCGAGACCACCAATACGACTTCGAG
KPM2403	ACGACAATTAGGTTCTGGGCGGACCCGGACATCTTCGAGACCACCAATACGACTTCGAG
KPM3012	ACCACCATCCGGTTCTGGGCGGACCCGACATCTTCGAGACCACCAAGTACGACTTCGAA
Bovine10	ACCACCATCCGGTTCTGGGCGGACCCGACATCTTCGAGACCACCAAGTACGACTTCGAA
KPM3101	ACCACGATCAGGTTCTGGGCGGACCCGACATCTTCGAGACCACCAAGTACGACTTCGAG
KPM3401	ACCACCATCAGGTTCTGGGCGGATCCGACATCTTCGAGACCACCAAGTACGACTTCGAG
ATCC51789	ACCACGTTCCGTTCTGGGCGGACCCGGACATCTTCGAGACGACGGATTACGACTTCGAG
T801	<u>TCAACGGTGCGGTTCTGGGCGGACCCGCTGTTTTCGAAACCACGGAATACGACTTCGAA</u>
T901	<u>TCAACGGTGCGGTTCTGGGCGGACCCGCTGTTTTCGAAACCACGGAATACGACTTCGAA</u>
T704	<u>TCAACGGTACGTTCTGGGCGGACCCGCTGTTTTCGAAACCACGGAATACGACTTCGAA</u>
T021	<u>TCAACGGTGCGGTTCTGGGCGGACCCGCTGTTTTCGAAACCACGGAATACGACTTCGAA</u>
KPM3504	ACGACGGTGCGGTTCTGGGCGGACCCAACGTTTTGAAACCACCAAGTACGACTTCGAA
KPM1001	ACGACGGTGCGGTTCTGGGCGGATCCCAATGTTTTGAGACCACCAAGTACGACTTCGAA 240

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Fig. 3

KPM2201 ACGGTGGCGCGCCGGCTGCAGGAGATGGCGTTCTGAACAAGGGTCTGACGATCAATCTG
 ATCC25274 ACGGTGGCGCGCCGGCTCCAAGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACTTG
 KPM1403 ACGGTGGCGCGCCGGTTGCAGGAAATGGCGTTCTGAACAAGGGCTTGACCATCAACCTC
 KPM2027 ACCGTGGCGCGCGGGCTGCAGGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTC
 KPM1201 ACGGTGGCGCGCGCTGCAGGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTC
 KPM2403 ACCGTGGCACGCGGGCTGCAGGAAATGGCATTCTGAACAAGGGCTTGACCATCAACCTC
 KPM3012 ACGGTGGCCCGCGGGCTGCAGGAAATGGCGTTCTGAACAAGGGCTTGACCATCAACCTC
 Bovine10 ACGGTGGCCCGCGGGCTGCAGGAAATGGCGTTCTGAACAAGGGCTTGACCATCAACCTC
 KPM3101 ACGGTGGCGCGCGGGCTGCAGGAAATGGCGTTCTGAACAAGGGTTGACCATCAACCTC
 KPM3401 ACGGTGGCGCGCGACTGCAGGAAATGGCGTTCTGAACAAGGGTTGACCATCAACCTC
 ATCC51789 ACGGTGGCACGCGGGCTGCAGGAAATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 T801 ACCGTGGCCCGCGGGCTGCAAGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 T901 ACCGTGGCCCGCGGGCTGCAAGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 T704 ACCGTGGCCCGCGGGCTGCAAGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 T021 ACCGTGGCCCGCGGGCTGCAAGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 KPM3504 ACCGTGGCGGACGGTTGCAGGAGATGGCGTTCTGAACAAGGGCTTGACCATCAACCTG
 KPM1001 ACCGTGGCACGCGTTGCAGGAGATGGCGTTCTGAACAAGGGCTTGACCATCAATCTG 300
 ** ** ** **

KPM2201 ACCGACGAACGCTCGAGCAGGACGAGGTTGTGACGAGGTCGTGACGACACCGCCGAA
 ATCC25274 ACCGACGAGCGGGTGGACGAGGACGAGGTCGTGATGAAGTCGTGACGACACCGCCGAT
 KPM1403 ACCGACGAACGTGTGAGCAGGACGAGGTTGTCGATGAGGTGTTAGCGACACCGCCGAG
 KPM2027 ACCGACGAACGAGTGGAGCAGGACGAGGTCGTGACGAGGTCGTGACGACACCGCCGAG
 KPM1201 ACCGACGAGCGGGTCACCCGAGGACGAGGTCGTGACGACGTCGTGATGATACCGCCGAA
 KPM2403 ACCGACGAGCGAGTTGCCAGGACGAGGTTGTGACGAGGTCGTGACGACACCGCCGAG
 KPM3012 ACCGACGAGCGGGTGACCAACGAAGAGGTCGTGACGAGGTTGTCGACGACACCGCCGAG
 Bovine10 ACCGACGAGCGGGTGACCAACGAAGAGGTCGTGACGAGGTTGTCGACGACACCGCCGAG
 KPM3101 ACCGACGAGCGGGTGAGCAACGAGGAGGTCGTGACGAGGTCGTGACGATACCGCCGAG
 KPM3401 ACCGACGAGCGGGTCAGTGAAGAGGAGGTCGTGACGATGTCGTGACGACACCGCCGAG
 ATCC51789 ACCGACGAGCGGGTGCGAAACGAAGAGGTCGTGACGAGGTCGTGACGACACCGCCGAG
 T801 ACCGACGAGAGGGTGACCAAGACGAGGTCGTGACGAAGTGGTCAGCGACGTCGCCGAG
 T901 ACCGACGAGAGGGTGACCAAGACGAGGTCGTGACGAAGTGGTCAGCGACGTCGCCGAG
 T704 ACCGACGAGAGGGTGACCAAGACGAGGTCGTGACGAAGTGGTCAGCGACGTCGCCGAG
 T021 ACCGACGAGAGGGTGACCAAGACGAGGTCGTGACGAAGTGGTCAGCGACGTCGCCGAG
 KPM3504 ACCGATCAGCGGGTAACCCAGGACGAAGTGGTCGACGAGGTTGTCGACGACGTCGCCGAG
 KPM1001 ACCGATCAGCGGGTGACCCAGGACGAGGTCGTGACGAGGTTGTCGACGACGTCGCCGAG 360

Fig. 4

KPM2201 GCGCCCAAATCCGCGAAGAGAAGGCTGCCGAATCCAAGGCCCGCACAAGGTCAAGCAG
 ATCC25274 GCGCCCAAAGTCCGCGAAGAGAAGGCGGCCGAATCCAAAGCGCCGCACAAGGTTAAGCAC
 KPM1403 GCGCCGAAGTCAGCCGAGGAGCAGGCGGCCGAATCGGCCAAGCGCACAAGGTCAAGCAC
 KPM2027 GCACCGAAGTCCGCGAAGAGAAGGCGCGGAATCGACTGCGCCACACAAGGTCAAGCAC
 KPM1201 GCACCAAAGTCCGCGCAGGAGAAGGCGGCCGAATCGACCGCGCGCACAAGGTCAAGAGC
 KPM2403 GCACCCAAAGTCCGCGAAGAAAAGGCGGCCGAATCCAAAGGGCGCATAAAGTTAAGCAC
 KPM3012 GCACCCAAAGTCCGCGCAGGAGAAGGCGGCCGAATCGGCTGCGCCGCATAAGGTCAAGCAC
 Bovine10 GCACCCAAAGTCCGCGCAGGAGAAGGCGGCCGAATCGGCTGCGCCGCATAAGGTCAAGCAC
 KPM3101 GCACCCAAAGTCCGCGCAGGAAAAGGCGGCCGAATCGACTGCGCCACATAAGGTTAAGCAC
 KPM3401 GCACCCAAAGTCCGCGCTAGAAAAAGCGGCCGAATCGACTGCGCCACACAAGGTTAAGCAC
 ATCC51789 GCGCCGAAGTCCGCGCGCAGAGAGGCGCGGAAGAAGCGGACCA—CGCAGAAAGTCAAGCAC
 T801 GCGCCGAAGTCCGCAAGTGAACGCGCAGCGGAATCCACTGCACCGCACAAAGTTAAGAGC
 T901 GCGCCGAAGTCCGCAAGTGAACGCGCAGCGGAATCCACTGCACCGCACAAAGTTAAGAGC
 T704 GCGCCGAAGTCCGCAAGTGAACGCGCAGCGGAATCCACTGCACCGCACAAAGTTAAGAGC
 T021 GCGCCGAAGTCCGCAAGTGAACGCGCAGCGGAATCCACTGCACCGCACAAAGTTAAGAGC
 KPM3504 GCCCCGAAGTCCGCGCAGTGAAGAAGGCGGCCGAATCCACCGCCCCCACAAGGTGAAGAAG
 KPM1001 GCCCCAAAGTCCGCGCAGCAGAGAAGGCGGCCGAATCCGCGCCCCCGCACAAGGTCAAGAAG 420

** ** ** ** ** ** ** ** ** * *** * ** ** ** ***
 ← Sequences No. 3, 5

KPM2201 CGCACCTTCCACTATCCCGGTGGTCTGGTGGACTTCGTCAAACACATCAACCGCACCAA
 ATCC25274 CGCACCTTCCACTACCGCGCGGCTTGGTGGACTTCGTCAAGCACATCAACCGGACCAAG
 KPM1403 CGCACGTTCCACTACCGGGTGGGTTGGTGGATTTGTCAGCACATCAATCGCACCAA
 KPM2027 CGCACCTTCCACTACCGCGGCGGTCTGGTGGACTTCGTCAAGCACATCAACCGCACCAAG
 KPM1201 CGCACCTTCCACTATCCCGGCGGTTTGGTGGATTTGTCAGCACATCAACCGCACCAAG
 KPM2403 CGCACTTTCCATTACCGCGCGGGCTGATCGACTTCGTCAAGCACATCAACCGGACCAAG
 KPM3012 CGCACCTTCCACTACCGCGGCGGCTGGTGGACTTCGTCAAACACATCAATCGCACCAA
 Bovine10 CGCACCTTCCACTACCGCGGCGGCTGGTGGACTTCGTCAAACACATCAATCGCACCAA
 KPM3101 CGCACCTTCCACTACCGCGGCGGCTGGTGGACTTCGTCAAGCACATCAACCGCACCAAG
 KPM3401 CGCACGTTCCACTACCGGGCGGCTTGGTGGACTTCGTCAAGCACATCAATCGGACCAAG
 ATCC51789 CGCACGTTCCATTACCGCGCGGCTTGGTGGATTTGTCAAACACATCAACCGCACAAAG
 T801 CGCACCTTTCACTATCCGGGTGGCCTGGTGGACTTCGTGAAACACATCAACCGCACCAAG
 T901 CGCACCTTTCACTATCCGGGTGGCCTGGTGGACTTCGTGAAACACATCAACCGCACCAAG
 T704 CGCACCTTTCACTATCCGGGTGGCCTGGTGGACTTCGTGAAACACATCAACCGCACCAAG
 T021 CGCACCTTTCACTATCCGGGTGGCCTGGTGGACTTCGTGAAACACATCAACCGCACCAAG
 KPM3504 CGTACCTTTCACTATCCCGGTGGCTTGGTTGACTTCGTCAAGCACATCAACCGCACCAAG
 KPM1001 CGTACCTTCCACTATCCCGGGGTCTGGTTGACTTCGTCAAGCACATCAACCGGACCAAG 480

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Fig. 5

KPM2201 AGCCCGATCCAACAGAGCGTCATCGACTTCGAAGGCAAAGGCACCGGCCACGAGGTCGAA
 ATCC25274 AGCCCGATCCAACAGAGCGTCATCGACTTCGAGGGCAAAGGCACCGGCCACGAGGTCGAG
 KPM1403 AACCCGATCCAGCAGAGCGTCATCGACTTCGACGGCAAAGGAACCGGGCACGAAGTCGAG
 KPM2027 AGCCCGATCCAGCAGAGCGTCATCGATTTGACGGCAAAGGCACCGGCCACGAGGTCGAG
 KPM1201 AGTCCGATTCAGCAGAGCATCGTCGACTTCGAGGGCAAAGGGCTCCGGCCACGAAGTCGAA
 KPM2403 AGCCCGATCCAGCAGAGTGTGTCGCTTCGACGGCAAAGGGTGAAGGGCACGAGGTCGAG
 KPM3012 AACCCCATCCAGCAGAGCATCATCGATTTGGTGGGAAGGGCCCGGCCACGAGGTCGAG
 Bovine10 AACCCCATCCAGCAGAGCATCATCGATTTGGTGGGAAGGGCCCGGCCACGAGGTCGAG
 KPM3101 AGCCCGATCCAGCAGAGCATCATCGACTTCGACGGCAAAGGTCCCGGCCACGAGGTCGAG
 KPM3401 AACCCGATTCACAACAGCATCGTGGATTTCTCGGCAAAGGGACCGGGCCACGAGGTCGAA
 ATCC51789 AACCCCATCCATTGAGCATCGTCGACTTCTCGGCAAAGGGTCCCGGCCACGAGGTCGAG
 T801 AACGCGATTTCATAGCAGCATCGTGGACTTTTCCGGCAAAGGGACCGGGCACGAGGTGGAG
 T901 AACGCGATTTCATAGCAGCATCGTGGACTTTTCCGGCAAAGGGACCGGGCACGAGGTGGAG
 T704 AACGCGATTTCATAGCAGCATCGTGGACTTTTCCGGCAAAGGGACCGGGCACGAGGTGGAG
 T021 AACGCGATTTCATAGCAGCATCGTGGACTTTTCCGGCAAAGGGACCGGGCACGAGGTGGAG
 KPM3504 AACGCCATCCACAGCAGCATCGTCGACTTCTCGGAAAGGGACCGGCCACGAAGTGGAG
 KPM1001 AACGCCATCCACAGCAGCATCGTCGACTTCTCGGTAAGGGACCGGGCCACGAAGTGGAG 540
 * * ** * * ** * * * * * * * * * *

KPM2201 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAATCGGTGCACACCTTCGCCAACACCATC
 ATCC25274 ATCGCGATGCAGTGGAACGGTGGCTACTCGGAGTCGGTGCACACCTTCGCCAACACCATC
 KPM1403 ATCGCGATGCAGTGGAACGGTGGTTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 KPM2027 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAGTCGGTGCACACCTTCGCCAACACCATC
 KPM1201 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAGTCGGTGCACACCTTCGCCAACACCATC
 KPM2403 ATCGCGATGCAGTGGAACGGCGGCTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 KPM3012 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAATCGGTGCACACCTTCGCCAACACCATC
 Bovine10 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAATCGGTGCACACCTTCGCCAACACCATC
 KPM3101 ATCGCGATGCAGTGGAACGGCGGCTACTCGGAATCGGTGCACACCTTCGCCAACACCATC
 KPM3401 ATCGCGATGCAGTGGAATGCCGGCTACTCGGAGTCGGTGCACACCTTCGCCAACACCATC
 ATCC51789 ATCGCAATGCAGTGGAACGCCGGCTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 T801 ATCGCGATGCAATGGAACGCCGGGTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 T901 ATCGCGATGCAATGGAACGCCGGGTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 T704 ATCGCGATGCAATGGAACGCCGGGTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 T021 ATCGCGATGCAATGGAACGCCGGGTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 KPM3504 ATCGCGATGCAGTGGAATGCCGGCTATTGGAAGTCGGTGCACACCTTCGCCAACACCATC
 KPM1001 ATCGCGATGCAGTGGAATGCCGGCTATTGGAAGTCGGTGCATACCTTCGCCAACACCATC 600

Fig. 6

KPM2201	AACACCCACGAGGGCGGCACCCACGAAGAGGGCTTCCGCAGTGCCTGACCTCGGTGGT
ATCC25274	AACACCCACGAGGGCGGTACGCACGAAGAAGGTTCCGCAGTGCCTGACCTCGGTGGT
KPM1403	AACACCCATGAGGGCGGCACCCACGAGGAGGGCTTCCGCAGCGCTGACCTCGGTGGT
KPM2027	AACACGCACGAGGGCGGCACCCACGAGGAGGGCTTCCGCAGCGCTGACCTCGGTGGT
KPM1201	AACACCCATGAGGGTGAACGCACGAAGAGGGCTTCCGCAGTGCCTGACCTCGGTGGT
KPM2403	AACACCCACGAGGGCGGCACCCACGAAGAAGGTTCCGCAGCGCTGACATCGGTGGT
KPM3012	AACACGCACGAGGGCGGCACCCACGAGGAGGGCTTCCGCAGCGCTGACCTCGGTGGT
Bovine10	AACACGCACGAGGGCGGCACCCACGAGGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
KPM3101	AACACCCACGAGGGCGGCACCCACGAAGAGGGCTTCCGCAGCGCTGACCTCGGTGGT
KPM3401	AACACCCACGAGGGCGGCACCCACGAAGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
ATCC51789	AACACCCACGAGGGCGGCACCCACGAAGAAGGTTCCGCAGCGCTGACCTCGGTGGT
T801	AACACCCACGAGGGCGGCACCCACGAAGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
T901	AACACCCACGAGGGCGGCACCCACGAAGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
T704	AACACCCACGAGGGCGGCACCCACGAAGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
T021	AACACCCACGAGGGCGGCACCCACGAAGAAGGCTTCCGCAGCGCTGACCTCGGTGGT
KPM3504	AACACCCATGAGGGCGGCACCCATGAAGAAGGTTCCGCAGCGCTGACCTCGGTGGT
KPM1001	AACACCCACGAGGGTGGGACCCACGAAGAGGGTTCCGCAGCGCTGACCTCGGTGGT 660

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KPM2201	AACAAGTACGCCAAAGACAAGAAGCTGCTCAAGGAGAAGGACCCGAATCTCACCGGTGAC
ATCC25274	AACAAATACGCCAAAGACAAGAAGCTGCTGAAAGACAAGGACCCGAACCTCACCGGTGAC
KPM1403	AACAAGTACGCCAAAGACAAGAAGCTGCTCAAGGACAAGGATCCCAACCTCACCGGCGAC
KPM2027	AACAAGTACGCCAAAGACAAGAAGCTGCTGAAGGACAAGATCCCAACCTCACCGGTGAC
KPM1201	AACAAGTACGCCAAAGACAAGAAGCTGCTCAAGGACAAGGACCCCAACCTCACCGGTGAC
KPM2403	AACAAGTACGCCAAAGACAAGAAGCTGCTCAAGGAGAAGGACGCCAACCTCACCGGCGAC
KPM3012	AACAAGTACGCCAAGGACAAGAAGCTGCTCAAGGACAAGGACCCCAACCTGACCGGCGAC
Bovine10	AACAAGTACGCCAAGGACAAGAAGCTGCTCAAGGACAAGGACCCCAACCTGACCGGTGAC
KPM3101	AACAAGTACGCCAAAGACAAGAAGTTGCTGAAAGACAAGGACCCGAACCTCACCGGCGAC
KPM3401	AACAAATACGCCAAGGACCGCAAACTCCTGAAGGACAAGGACCCCAACCTCACCGGCGAC
ATCC51789	AACAAGTACGCCAAGGACCGAAAAGCTGCTGAAGGACAAGGACCCCAACCTCACCGGCGAC
T801	AACAAGTACGCCAAGGACCGCAAGCTACTGAAGGACAAGGACCCCAACCTCACCGGTGAC
T901	AACAAGTACGCCAAGGACCGCAAGCTACTGAAGGACAAGGACCCCAACCTCACCGGTGAC
T704	AACAAGTACGCCAAGGACCGCAAGCTACTGAAGGACAAGGACCCCAACCTCACCGGTGAC
T021	AACAAGTACGCCAAGGACCGCAAGCTACTGAAGGACAAGGACCCCAACCTCACCGGTGAC
KPM3504	AACAAGTACGCCAAGGACCGCAAACTGCTCAAAGACAAGGACCCCAACCTCACCGGCGAC
KPM1001	AACAAGTACGCCAAGGACCGCAAACTGCTCAAGGAAAAGGACCCCAACCTCACCGGCGAC 720

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Fig. 7

KPM2201 GACATCCGGGAGGGGTTGGCCGCGGTGATCTCGGTGAAGGTCGCCAACCAGGATTCGAG
 ATCC25274 GACATCCGGGAGGGGACTGGCCGCGGTGATCTCGGTCAAGGTCGCCAACCAGGATTCGAG
 KPM1403 GACATCCGAGAAGGGCTGGCCGCGGTGATCTCGGTGAAGGTCGCCAAGCCAGGATTCGAG
 KPM2027 GACATCCGTGAGGGCTTGGCCGCGGTGATCTCGGTGAAGGTCGCCAAGCCAGGATTCGAA
 KPM1201 GACATCCGCGAGGGGTTGGCCGCGGTGATCTCGGTGCGGGTGGCAGAGCCAGGATTCGAG
 KPM2403 GACATTCGCGAGGGGCTGGCCGCGGTGATCTCGGTGAAAGTTGCCAACCAGGATTCGAG
 KPM3012 GACATCCGCGAGGGTTTGGCCGCGGTGATCTCGGTCAAGGTGAGCGAACCAGGATTCGAG
 Bovine10 GACATCCGCGAGGGTTTGGCCGCGGTGATCTCGGTCAAGGTGAGCGAACCAGGATTCGAG
 KPM3101 GACATTCGCGAAGGCTGGCCGCGGTGATCTCGGTCAAGGTGAGCGAACCAGGATTCGAG
 KPM3401 GACATCCGGGAAGGCTGGCAGCGGTGATTTCCGTCAAGGTGAGCGAACCAGGATTCGAG
 ATCC51789 GACATTCGTGAGGGCTGGCCGCGGTGATCTCGGTCAAGGTGAGCGAACCAGGATTCGAG
 T801 GATATCCGGGAAGGCTGGCCGCTGTGATCTCGGTGAAGGTGAGCGAACCAGGATTCGAG
 T901 GATATCCGGGAAGGCTGGCCGCTGTGATCTCGGTGAAGGTGAGCGAACCAGGATTCGAG
 T704 GATATCCGGGAAGGCTGGCCGCTGTGATCTCGGTGAAGGTGAGCGAACCAGGATTCGAG
 T021 GATATCCGGGAAGGCTGGCCGCTGTGATCTCGGTGAAGGTGAGCGAACCAGGATTCGAG
 KPM3504 GACATCCGGGAAGGTTGGCCGCGGTGATTTCCGTCAAGGTGAGCGAACCAGGATTCGAG
 KPM1001 GACATCCGGGAAGGTTGGCCGCGGTGATTTCCGTCAAGGTGAGCGAACCAGGATTCGAG 780
 ** * * * * * ** ** ** ** ** * * * * *

KPM2201 GGTGAGACCAAGACCAAGCTGGGCAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGC
 ATCC25274 GGCCAGACAAAGACCAAGCTGGGCAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGC
 KPM1403 GGCCAGACTAAGACGAACTGGGCAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGT
 KPM2027 GGCCAGACCAAGACCAAGCTGGGCAACACCGAGGTGAAGTCGTTGTCAGAAAGGTGTGC
 KPM1201 GGTGAGACCAAGACCAAGCTGGGCAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGT
 KPM2403 GGCCAGACCAAGACCAAGCTGGGTAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGC
 KPM3012 GGCCAGACCAAGACCAAGCTGGGCAACACCGAGGTGAAGTCGTTGTCAGAAAGGTGTGC
 Bovine10 GGCCAGACCAAGACCAAGCTGGGCAACACCGAGGTGAAGTCGTTGTCAGAAAGGTGTGC
 KPM3101 GGTGAGACCAAGACCAAGCTGGGCAACACCGAAGTGAAGTCGTTGTCAGAAAGGTGTGC
 KPM3401 GGCCAGACCAAAACCAAGCTGGGCAACACCGAGGTCAAGTCGTTGTCAGAAAGGTGTGC
 ATCC51789 GGCCAGACCAAAACCAAGCTGGGCAACACCGAAGTCAAGTCGTTGTCAGAAAGGTGTGC
 T801 GGCCAGACCAAGACCAAGTTGGGCAACACCGAGGTCAAATCGTTTGTGAGAAAGGTCTGT
 T901 GGCCAGACCAAGACCAAGTTGGGCAACACCGAGGTCAAATCGTTTGTGAGAAAGGTCTGT
 T704 GGCCAGACCAAGACCAAGTTGGGCAACACCGAGGTCAAATCGTTTGTGAGAAAGGTCTGT
 T021 GGCCAGACCAAGACCAAGTTGGGCAACACCGAGGTCAAATCGTTTGTGAGAAAGGTCTGT
 KPM3504 GGCCAGACCAAGACGAACTAGGCAACACCGAGGTGAAGTCGTTGTCAGAAAGGTGTGC
 KPM1001 GGCCAGACCAAGACGAACTGGGCAACACCGAGGTGAAGTCGTTGTCAGAAAGGTGTGC 840
 ** * * * * * ** ** ** * * * * * ** ** * * * * * ** * *

Fig. 8

KPM2201	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCTAAAACCGTTGTGAAC
ATCC25274	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTTGTCAAC
KPM1403	AACGAACAACCTCACTCACTGGTTGAGGCCAATCCGTGGAAGCTAAAACCGTTGTAAAC
KPM2027	AACGAGCAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
KPM1201	AACGAGCAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGATTGTGAAC
KPM2403	AACGAACAGCTGACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
KPM3012	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
Bovine10	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
KPM3101	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
KPM3401	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
ATCC51789	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
T801	<u>AACGAACAGCTGACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC</u>
T901	<u>AACGAACAGCTGACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC</u>
T704	<u>AATGAACAGCTGACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC</u>
T021	<u>AACGAACAGCTGACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC</u>
KPM3504	AATGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC
KPM1001	AACGAACAGCTCACCCTACTGGTTGAGGCCAATCCGTGGAAGCCAAAACCGTGGTGAAC 900
	<div style="display: flex; justify-content: space-between; align-items: center;"> <div> <p>← ** ** ** **</p> <p>Sequences No. 51, 57</p> </div> <div> <p>← ** * ** * **</p> <p>Sequences No. 47, 53</p> </div> </div>
KPM2201	AAAGCGGTGTGTCGTCGCGCCAGGCGCGGATCGCCGCGCGCAAGGCGCGAGAGCTGGTGC
ATCC25274	AAGGCGGTTTCTGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM1403	AAGGCGGTTTCTGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM2027	AAAGCGGTGTGTCGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM1201	AAGGCGGTATCCTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM2403	AAGGCGGTCTGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM3012	AAGGCGGTTTCATCAGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
Bovine10	AAGGCGGTTTCATCAGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM3101	AAGGCGGTGTGTCGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM3401	AAGGCGGTTTCTGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
ATCC51789	AAAGCGGTGTGTCGTCGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
T801	AAGGCTGTGTCTCGGCGCAAGCCCGTATCGCGGCAGTAAGGCACGAGAGTTGGTGC
T901	AAGGCTGTGTCTCGGCGCAAGCCCGTATCGCGGCAGTAAGGCACGAGAGTTGGTGC
T704	AAGGCTGTGTCTCGGCGCAAGCCCGTATCGCGGCAGTAAGGCACGAGAGTTGGTGC
T021	AAGGCTGTGTCTCGGCGCAAGCCCGTATCGCGGCAGTAAGGCACGAGAGTTGGTGC
KPM3504	AAGGCASTTTCATCGGCGCAGGCGCGGATCGCGCGCGGAAAGGCGCGAGAGTTGGTGC
KPM1001	AAGGCGGTTTCATCGGCGCAAGCAGCATTGCGCGCGCGCAAGGCGCGAGAGTTGGTGC 960
	<div style="display: flex; justify-content: space-between; align-items: center;"> <div> <p>** ** ** **</p> </div> <div> <p>* * * * *</p> </div> </div>

Fig. 9

KPM2201 CGCAAGAGCGCAACCGACCTCGGCGGGCTGCCGGGCAAGCTGCCGACTGCCGTTCCAGC
 ATCC25274 CGCAAGAGCGCGACCGATTTGGGCGGGCTGCCGGCAAGCTGCCGACTGCCGTTCCACC
 KPM1403 CGTAAGAGTGCTACGGATTTGGGTGGGTGCCGGGCAAGTTGGCTGATTGCCGCTCGACG
 KPM2027 CGCAAGAGCGCCACCGACCTCGGCGGTCTGCCGGGAAAGCTGCCGACTGCCGCTCCACC
 KPM1201 CGCAAGAGCGCAACCGATCTCGGTGGGTGCCGGGCAAGTTGCCGACTGCCGCTCGACA
 KPM2403 CGCAAGAGCGCTACCGATCTCGGTGGGTGCCGGGCAAGCTGCCGACTGCCGCTCCACC
 KPM3012 CGCAAGAGCGCAACCGACCTGGGCGGGCTGCCGGGCAAGCTGCCGACTGCCGCTCGACC
 Bovine10 CGCAAGAGCGCAACCGACCTGGGCGGGCTGCCGGGCAAGCTGCCGACTGCCGCTCGACC
 KPM3101 CGCAAGAGCGCCACCGATCTGGGCGGGCTGCCGGGCAAGCTGCCGACTGCCGCTCGACG
 KPM3401 CGCAAGAGCGCCACCGACCTCGGTGGGTGCCGGGTAAGCTGCCGACTGCCGCTCCACC
 ATCC51789 CGCAAGAGCGCAACCGATCTTGGGCGGGCTGCCGGGCAAGCTGCCGACTGCCGCTCGACC
 T801 CGTAAGAGCGCCACCGACATCGGTGGATTGCCGGGCAAGCTGCCGATTGCCGTTCCACG
 T901 CGTAAGAGCGCCACCGACATCGGTGGATTGCCGGGCAAGCTGCCGATTGCCGTTCCACG
 T704 CGTAAGAGCGCCACCGACATCGGTGGATTGCCGGGCAAGCTGCCGATTGCCGTTCCACG
 T021 CGTAAGAGCGCCACCGACATCGGTGGATTGCCGGGCAAGCTGCCGATTGCCGTTCCACG
 KPM3504 CGCAAGAGCGCAACCGATCTGGGCGGACTACCGGGCAAGTTGCCGACTGCCGCTCGACC
 KPM1001 CGCAAGAGCGCAACCGATCTGGGCGGACTACCGGGCAAGCTGCCGACTGCCGCTCGACC 1020

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KPM2201 GATCCCGCAAATCCGAAGTGTATGTGGTGGAGGGGACTCCGCCGGCGGCTCGGCCAAG
 ATCC25274 GACCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCAGGTGGCTCGGCCAAG
 KPM1403 GATCCGCGGAAATCTGAGCTGTATGTGGTGGAGGGTGATTCCGCCGGTGGGTCCGCCAAG
 KPM2027 GACCCGCGGAAATCCGAAGTGTATGTGGTGGAGGGGATTCGCCGGCGGCTCGGCCAAG
 KPM1201 GATCCGCGTAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGCTCGGCCAAG
 KPM2403 GATCCGCGCAAGTCCGAATTGTATGTGGTGGAGGGGACTCGGCCGGCGGCTCGGCCAAG
 KPM3012 GACCCGCGCAAGTCCGAATTGTATGTGGTGGAGGGTGACTCGGCCGGCGGCTCGGCCAAG
 Bovine10 GACCCGCGCAAGTCCGAATTGTATGTGGTGGAGGGTGACTCGGCCGGCGGCTCGGCCAAG
 KPM3101 GATCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGATTCCGCCGGCGGCTCGGCCAAG
 KPM3401 GACCCGCGAAATCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGCTCGGCCAAG
 ATCC51789 GATCCACGCAAGTCCGAATTGTATGTGGTGGAGGGTGATTCCGCCGGCGGCTCGGCCAAG
 T801 GATCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGTTCTGCAAAA
 T901 GATCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGTTCTGCAAAA
 T704 GATCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGTTCTGCAAAA
 T021 GATCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGACTCGGCCGGCGGTTCTGCAAAA
 KPM3504 GACCCCGTAAGTCCGAATTATATGTGGTGGAGGGTGATTGAGCCGGCGGCTCGGCCAAG
 KPM1001 GACCCGCGCAAGTCCGAAGTGTATGTGGTGGAGGGTGATTGAGCCGGCGGCTCGGCCAAG 1080

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Continued on p. 12

Fig. 10

KPM2201	AGCGGTCGGGATTGATGTTCCAGGCGATTCTTCCGTTGCGCGGCAAGATCATCAACGTC
ATCC25274	AGCGGCGGTGACTCGATGTTCCAGGCCATCCTGCCGCTGCGCGGCAAGATCATCAACGTC
KPM1403	AGTGGGCGTGATTGATGTTCCAGGCGATCTTGGCGCTGCGCGGCAAGATCATCAACGTC
KPM2027	AGCGGGCGGACTCGATGTTCCAGGCGATCCTGCCGCTGCGCGGCAAGATCATCAATGTC
KPM1201	AGTGGCGCGGATTGATGTTCCAGGCGATCCTGCCGCTGCGCGGCAAGATCATCAATGTC
KPM2403	AGCGGCCGCGACTCGATGTTCCAGGCGATACTTCCGTTGCGCGGCAAGATCATCAACGTC
KPM3012	AGCGGCCGGGACTCGATGTTCCAGGCCATCCTTCCGCTGCGCGGCAAGATCATCAACGTC
Bovine10	AGCGGCCGGGACTCGATGTTCCAGGCCATCCTTCCGCTGCGCGGCAAGATCATCAACGTC
KPM3101	AGCGGCCGCGACTCGATGTTCCAGGCCATCCTGCCGCTGCGCGGCAAGATCATCAACGTC
KPM3401	AGCGGCCGCGACTCGATGTTCCAGGCGATCCTCCGCTGCGTGGCAAGATCATCAACGTC
ATCC51789	AGCGGCCGCGACTCGATGTTCCAGGCGATCCTGCCGTTGCGGGGCAAGATCATCAACGTC
T801	AGCGGTGCGGATTGATGTTCCAGGCGATACTTCCGCTGCGCGGCAAGATCATCAATGTG
T901	AGCGGTGCGGATTGATGTTCCAGGCGATACTTCCGCTGCGCGGCAAGATCATCAATGTG
T704	AGCGGTGCGGATTGATGTTCCAGGCGATACTTCCGCTGCGCGGCAAGATCATCAATGTG
T021	AGCGGTGCGGATTGATGTTCCAGGCGATACTTCCGCTGCGCGGCAAGATCATCAATGTG
KPM3504	AGCGGCCGCGACTCGATGTTCCAGGCGATCTTCCGTTGCGCGGCAAGATCATCAACGTC
KPM1001	AGCGGTGCGGACTCGATGTTCCAGGCCATCTTCCGTTGCGCGGCAAGATCATCAACGTC 1140
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KPM2201	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
ATCC25274	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM1403	GAAAAGGCCCGCATCGATCGGGTGCTGAAAAACACCGAAGTCCAGGCCATCATCACCGGG
KPM2027	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM1201	GAAAAGGCACGCATCGACCGAGTCTGAAAAACACTGAAGTCCAGGCCATCATCACCGGG
KPM2403	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM3012	GAAAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
Bovine10	GAAAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM3101	GAGAAGGCCCGCATCGACCGGGTGTTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM3401	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
ATCC51789	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACTGAGGTCCAGGCCATCATCACCGGG
T801	GAGAAAGCGCGCATCGACCGGGTGCTAAAGAACACCGAAGTCCAGGCCATCATCACCGGG
T901	GAGAAAGCGCGCATCGACCGGGTGCTAAAGAACACCGAAGTCCAGGCCATCATCACCGGG
T704	GAGAAAGCGCGCATCGACCGGGTGCTAAAGAACACCGAAGTCCAGGCCATCATCACCGGG
T021	GAGAAAGCGCGCATCGACCGGGTGCTAAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM3504	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG
KPM1001	GAGAAGGCCCGCATCGACCGGGTGCTGAAGAACACCGAAGTCCAGGCCATCATCACCGGG 1200
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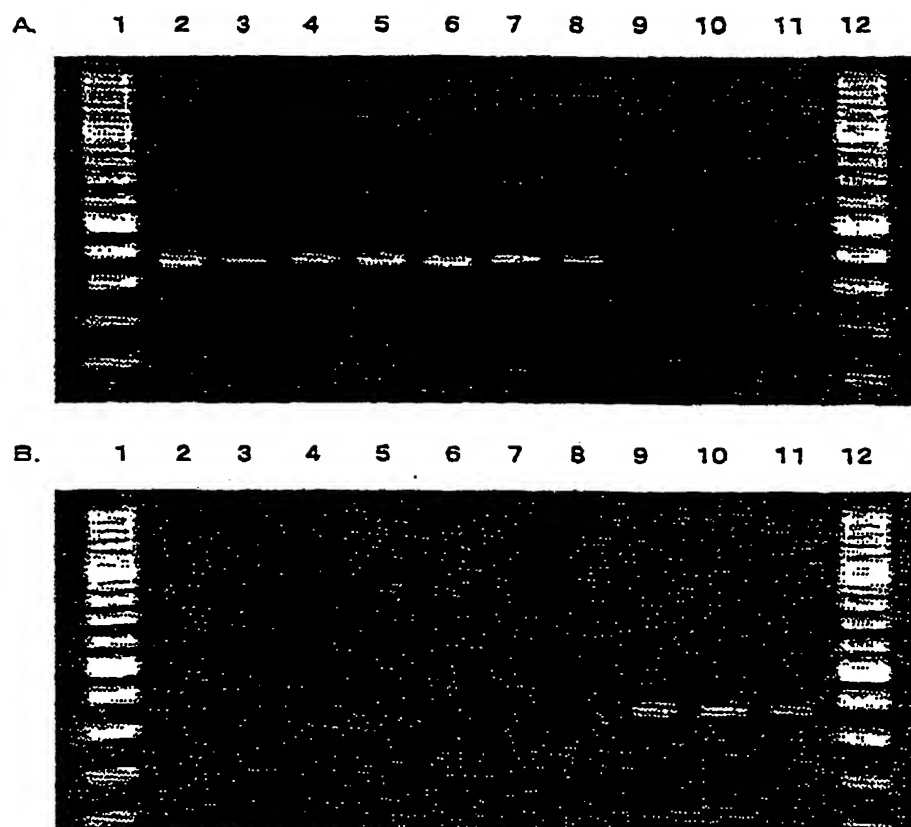
Fig. 11

KPM2201 CTGGGCACCGGGATCCACGACGAGTTGACATCACCAAAGCTGCGCTACCACAAGATCGTA
 ATCC25274 CTGGGTACCGGTATTACGACGAGTTGACATTTCTAAAGTGCCTTACCACAAGATCGTG
 KPM1403 CTGGGCACCGGCATCCACGACGAAATTCGACATCACCAAAGCTGCGCTTACCACAAGATCGTG
 KPM2027 CTGGGTACCGGGATTACGACGAGTTGACATCACCAAGCTGCGCTATCACAAGATCGTG
 KPM1201 TTGGGTACCGGTATTACGACGAAATTCGACCTCTGAAAGCTGCGCTATCACAAGATCGTC
 KPM2403 CTGGGTACCGGAATTACGACGAGTTGACCTCGCCAAAGCTGCGCTACCACAAGATCGTG
 KPM3012 CTGGGCACCGGGATTACGACGAGTTGACATCACCAAGCTGCGCTACCACAAGATCGTG
 Bovine10 CTGGGCACCGGGATTACGACGAGTTGACATCACCAAGCTGCGCTACCACAAGATCGTG
 KPM3101 CTGGGCACCGGCATCCACGACGAGTTGACATCACCAAGCTGCGCTATCACAAGATCGTG
 KPM3401 CTGGGCACCGGGATTACGACGAGTTGACATCACCAAGCTCGGTACCACAAGATCGTG
 ATCC51789 CTGGGCACCGGGATTACGACGAGTTGACATCTCAAGCTGCGCTACCACAAGATCGTG
 T801 CTGGGCACCGGGATCCACGACGAGTTGATATCGGCAAGCTGCGCTACCACAAGATCGTG
 T901 CTGGGCACCGGGATCCACGACGAGTTGATATCGGCAAGCTGCGCTACCACAAGATCGTG
 T704 CTGGGCACCGGGATCCACGACGAGTTGATATCGGCAAGCTGCGCTACCACAAGATCGTG
 T021 CTGGGCACCGGGATCCACGACGAGTTGATATCGGCAAGCTGCGCTACCACAAGATCGTG
 KPM3504 TTGGGCACCGGTATTACGACGAAATTCGACATCGCGAGACTGCGTTACCACAAGATCGTG
 KPM1001 TTGGGTACCGGCATCCACGACGAAATTCGACATCGCGAGACTGCGTTACCACAAGATCGTG 1260
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KPM2201	TTG	KPM1403	M. simiae
ATCC25274	TTG	KPM1201	M. marinum
KPM1403	TTG	KPM2201	M. gordonae
KPM2027	CTG	ATCC25274	M. asiaticum
KPM1201	TTG	KPM2027	M. scrofulaceum
KPM2403	CTG	KPM2403	M. szulgai
KPM3012	TTG	KPM3012	M. avium
Bovine10	TTG	Bovine10	M. paratuberculo
KPM3101	CTG	KPM3101	M. intracellular
KPM3401	CTG	KPM3401	M. malmoense
ATCC51789	CTG	ATCC51789	M. branderi
T801	CTG	T801	M. africanum
T901	CTG	T901	M. microti
T704	CTG	T704	M. bovis
T021	CTG	T021	M. tuberculosis
KPM3504	CTG	KPM3504	M. gastri
KPM1001	CTC	KPM1001	M. kansasii

*

Fig. 12



Phylogenetic tree showing relationships between *M. marinum* (KPM1201), *M. atlanticum* (ATCC25274), *M. scrofulaceum* (KPM2027), *M. gordonae* (KPM2020), *M. szulgai* (KPM2403), and *M. slimiae* (KPM1403). Two clusters of new species are highlighted with stippled ovals: one containing *M. gordonae* and *M. scrofulaceum*, and another containing *M. szulgai* and *M. slimiae*. The label "New species" is placed to the right of the tree.

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Fig. 14

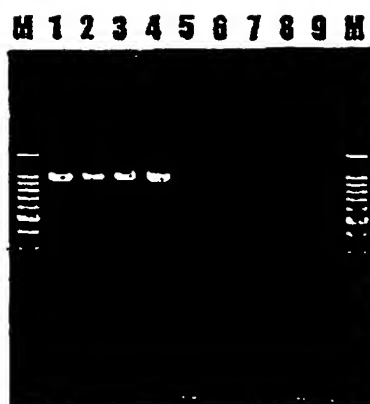


Fig. 15

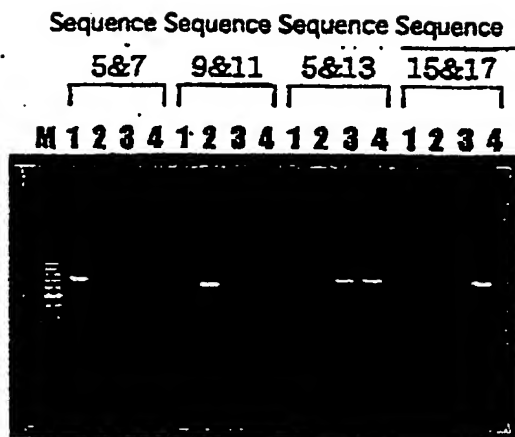
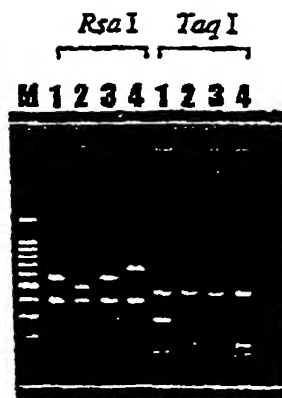


Fig. 16



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